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CARCINOMA IN OSTEOMYELITIS

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THAT carcinoma may develop in old ulcers and sinuses has been known for about a hundred years, but little has been written about the subject recently.

To Marjolin, in 1828, must go the credit for having first recognized malignant changes in old ulcers, but whether or not he described carcinoma in old sinuses is uncertain.[1] According to Boegehold, Marjolin designated such malignant change as "warty ulcer."

Caesar Hawkins, surgeon to St. George's Hospital in London, read a paper in 1833 entitled "Cases of Warty Tumors in Cicatrices." He reported 7 cases, most of them arising from burns, flogging, or other deep scars. One case, however, seems quite definitely to have followed osteomyelitis. The record was as follows:

"James Calcott, aet. 49, was admitted into St. George's Hospital, May 28, 1828, under the care of Sir Benjamin Brodie.

"He had a yellow, wart-like fungus, about the size of a crown piece, which rose above the skin, and through which some bone was felt; this was situated in the center of some old cicatrices. He had received a blow on the shin from an anchor 27 years previous to his admission, which was followed by a large abscess, out of which some dead bone had been taken while in a naval hospital, after which the wound healed. Fourteen months ago he received another injury, which was also succeeded by an abscess, at the bottom of which the bone was exposed. The exposed bone was believed to be dead, but as it was not loose, he left the hospital until it was in a fit state to be removed; soon after the fungus formed, and he was re-admitted, when the tumor seemed to be connected with the bone or the periosteum, or both.

"June 5th, the tumor being removed with the periosteum, to which it was fixed, a portion of the bone which seemed to be more vascular than usual was taken away with the trephine, so as to expose the medullary canal. The vascularity did not extend more than a quarter of an inch in depth, and the bone was not otherwise altered. The wound healed well, and the man has since continued free from disease."

This history corresponds closely to many subsequently reported and to those in this series. As to the prognosis of such "warty tumors," Hawkins was most sanguine, "quieting his own and his patient's anxiety by a confident assurance that the disease is not in the least malignant, as cancer is malignant, but on the contrary entirely local in its origin and does not contaminate even the adjacent parts, except in a very trifling degree, so that no future mischief need be apprehended." Although such a particularly favorable prognosis is probably not justified, it is generally recognized that carcinoma developing in scars or sinuses is usually of low grade malignancy.

The next case is that reported by Dittrich in 1847. The patient was a man of 38, who had suffered from necrosis of the tibia for 20 years. A thigh amputation was performed. The lesion involved the lower three-fourths of the tibia. The specimen was examined by Professor Rokitansky, who confirmed the diagnosis

[1] Marjolin's article in the Dict. de méd. for 1828 could not be obtained in Boston or Washington.

of carcinoma. He found epithelial cells growing down the sinus tract deep into the cavity of the bone. Although he could find no macroscopic evidence of cancer at the mouth of the sinus, he believed it probable that epithelial cells had grown in from the surface and had caused the disease. This is in accord with our present belief, it being not at all uncommon to find malignant epithelial cells at the mouth of the sinus extending deep into the cavity.

In the next 40 or 50 years quite a few cases of cancer in osteomyelitis were reported, among them cases by Hannover (1855), Cornil and Ranvier (1866), Winiwater (1878), Nicoladini (1881), Fischer (1881), Esmarch, Volkmann (1889), Van Hook (1890), and Feigel (1891).

In 1891, Borchers collected a series of 20 cases from the literature and added 5 from records and patients under his observation. Of the 25 cases collected 14 followed acute osteomyelitis, but the others may have been tuberculosis. Borchers noted that metastasis was rare; in none of his cases were there metastases beyond the regional lymph nodes. He saw many patients well several years after amputation.

In 1894, von Friedlander reported 3 cases. In the same year Devars collected a series of 39 cases. He noted how very much more frequently the tibia was involved than any other bone, 26 times out of 39 cases. Of the other bones the femur was affected five times, the bones of the foot five times, the arm twice, and the knee once. He also noted, as is the case in this series, two very different clinical varieties of the disease. "Sometimes," he writes, "there exists in the nearby skin a more or less extensive cancerous ulcer which puts one at once on the track of the diagnosis; at other times, on the contrary, the lesion is produced deep within the tissues, there is no trace of epithelioma at the level of the fistula, and it is then that only a complete examination, noting the peculiar foulness of the discharge . . . can put one on the track of the diagnosis." Devars found involvement of the lymph glands in many cases, a finding which does not seem to be substantiated by most authorities, or by our own series.

During the next 10 years, from 1894 to 1904, there was much interest in the subject, judging from the number of cases reported. Cone, in 1897, reported 2 cases with special reference to the pathological findings. In 1898, Verdelet reported a case involving the fibula. In 1899, Crutchet and Lanelongue each reported cases. Cargue and Bauby in 1902, and Guiot in 1904, wrote very good dissertations on the subject with reviews of the literature, case reports, and general discussions of the course and treatment of the disease. In 1903, Sherrill reported a case, noting its slow progress and advising amputation.

From that time up to the present there has been almost nothing written about cancer in osteomyelitis, with the exception of case reports by Mathieu and Khan in 1920, by Hitzrot in 1921, and by Vernengo in 1928. Amputation was necessary in all these cases. Vernengo urged as a prophylactic measure that every effort be made to cure fistulæ in bone.

Our interest in this subject has been recently stimulated by the occurrence of the following case:

CASE 1. P. Z., a single man of 58 years (E. S. No. 305300) entered the hospital on March 12, 1930, because of pain in the left knee of about 20 years' duration. Twenty years ago he had been prostrated with swelling and pain in both legs, after which motion had been limited in both knees. A sinus in the left thigh had been discharging pus almost continuously for the entire 20 years.

Physical examination showed both femora and tibiæ greatly thickened with nearly complete ankylosis of both knees. Along the lateral aspect of the distal portion of the left thigh were two large sinuses draining foul, purulent material. X-ray examination showed chronic osteomyelitis of the left femur and both tibiæ. Incision and curettage of the left femur was done a few days after admission and revealed an enormous, necrotic cavity containing very friable and porky material. Pathological report showed chronic osteomyelitis and epidermoid carcinoma, grade I.

Accordingly, in view of the extent and character of the disease in the left femur, a hip joint disarticulation was decided upon, and performed by Dr. R. H. Sweet about 2 weeks after admission, following which the patient made an uneventful recovery.

This case is one of the few in our series in which carcinoma was not suspected before operation, and even in this case there was a slight epithelial hyperplasia at the sinus opening (Fig. 1) which subsequent examination showed to be carcinoma. The gross appearance of the cavity and sinus is shown in the accompanying illustrations (Figs. 1 and 2).

After disarticulation the femur and tibia were split longitudinally, showing the extent of the disease (Figs. 3 and 4). In spite of the most careful X-ray pictures taken both before and after disarticulation,

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 4.

Fig. 1. Sinus opening shows definite epithelial hyperplasia. Clinically suspicious of carcinoma. Microscopic examination showed epidermoid carcinoma. Case 1.

Fig. 2. General view of sinus after curettage, showing friable, necrotic material at base. Case 1.

Fig. 3. Appearance of cavity after splitting the femur. Probe inserted in sinus tract. Carcinoma lining nearly the entire cavity and infiltrating the bone in some places to a depth of an inch and a half. Case 1.

Fig. 4. General appearance of split femur and tibia. The dark area at the upper end of the femur is merely hæmorrhagic bone marrow. The probe is inserted in the carcinoma osteomyelitis cavity. The tibia shows only osteomyelitis. Case 1.

it was impossible to discover anything definite in the plates which would have led to a diagnosis of carcinoma (Figs. 5 and 6).

On searching the hospital records, 10 other cases were discovered, in 5 of which the carcinoma was obvious on physical examination, and amputation was performed in every case. The following are summaries of these 5 cases:

Case 2. O. M., a man of 61 years (S. R. Vol. 377, p. 216) entered the hospital on June 10, 1901, because of pain in the left leg. He had been more or less of a cripple all his life, his left foot having become swollen at the age of 4 years, and having been filled with discharging sinuses since childhood. Examination showed the left foot to be "one mass of foul ulcer, from which as a base grows a cauliflower mass. Tibia up to upper third is thickened and shows several scars of old sinuses."

Amputation one inch below the knee was performed 2 days later by Dr. S. J. Mixter, under ether anæsthesia. The following day it was necessary to open the stump to control a postoperative hæmorrhage. Although the wound did well, the patient ran a septic temperature without apparent cause, finally developing a hypostatic pneumonia from which he died 30 days after operation.

Pathological report showed papillary epidermoid carcinoma of the leg and ankle.

This is the only immediate mortality in the series, and death apparently was due entirely to the complicating pneumonia.

Case 3. A. W. M., a widower of 50 years (E. S. No. 144424) entered the hospital on September 19, 1905, because of a sore on his left leg, which had been present for the past 36 years, since the patient had typhoid fever at the age of 14. The sore had never completely healed, and had discharged dead bone at times ever since the onset. About 2 years before entry, he had received a blow on this sore spot, since which time he had been unable to work, and the leg had discharged continually. Physical examination showed at the upper third of the left tibia a sloughing dirty sore, covering the whole front of the leg with a mass in the center the size of a small plum. The day after admission a mid-thigh amputation was performed by Dr. R. B. Greenough and 10 days later the groin was dissected. Pathological report showed epithelioma of leg, the glands from the groin being negative. Convalescence was uneventful. One year later he was examined and found to have a perfect result.

Case 4. W. H. B., a widower of 75 years (E. S. No. 154148) entered on August 2, 1907, because of pain in the left lower leg, and lameness of 6 months' duration. When 11 years old he had had a "fever sore" on his leg, which had been lanced and pieces of bone had been removed. After a period of alternate healing and breaking down, it had remained healed for 25 years. It then broke open again, and bone fragments were again discharged a year and a half before admission. Examination (Fig. 7) showed a cauliflower reddish mass with a foul discharge, involving almost the whole anterior surface of the left lower leg. A few days after admission a low thigh amputation was performed by Dr. Hugh Williams. The pathological examination showed

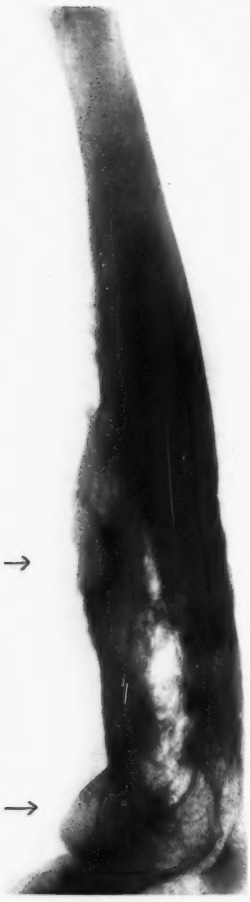

Fig. 5.

Fig. 5. Anteroposterior and lateral X-ray pictures of the femur taken immediately after hip joint disarticulation. Carcinomatous areas indicated between arrows. Case 1.

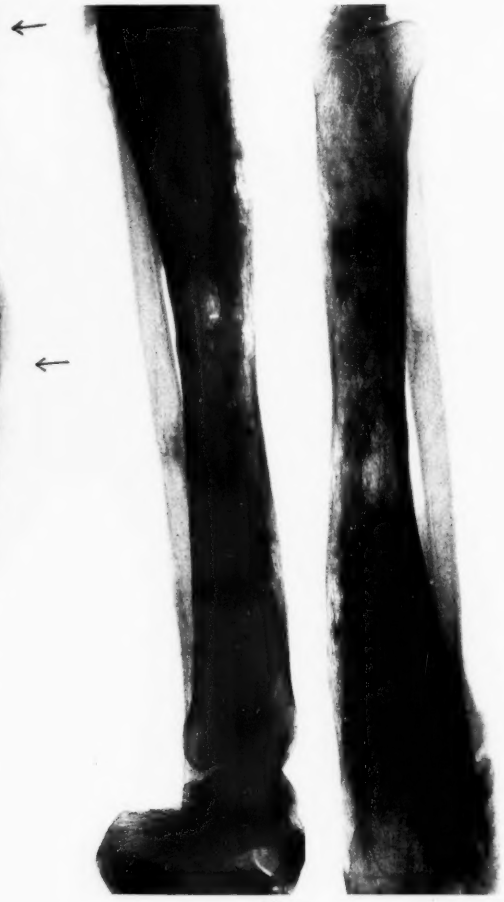

Fig. 6.

Fig. 6. Anteroposterior and lateral X-ray pictures of tibia, showing extensive osteomyelitis. No carcinoma present in tibia. Case 1.

epithelioma. Convalescence was uneventful except for slight wound sepsis. One year later this patient was examined and found to have a well healed stump with no evidence of recurrence.

Case 5. P. D., a single white male of 38 years (W. S. No. 269892) entered the hospital May 23, 1925, for treatment of a growth on his right foot. Twenty-six years previously he had lost the distal part of his foot by having it run over by a railroad train. One year ago a sinus had opened over the end of the first metatarsal and had discharged pus and a small piece of bone. This sinus had failed to heal. Physical examination showed over the tip of the fifth metatarsal a soft, broad, fungating lesion about 2 centimeters in diameter, producing a foul smelling discharge. A Symes amputation was performed by Dr. Beth Vincent a few days after admission, with biopsy of a right inguinal gland. Microscopic examination of the tumor showed squamous cell carcinoma containing many pearls. The lymph node was negative. The patient made an uneventful recovery except for some wound sepsis, and a somewhat painful amputation stump. Two years later he was examined in the tumor clinic, where no evidence of recurrence could be noted.

Case 6. *First admission.* A. R. G., a married man of 29 years (W. S. Vol. 307, p. 98) entered through the Emergency Ward on December 21, 1895, because of a crushed right foot, the injury

having been caused by the door of a street car a few hours previously. Examination showed the skin on the dorsum of the foot entirely dissected off, a compound fracture of the fifth metatarsal, and lacerations and crushing of the soft parts. After a long and somewhat stormy convalescence the patient was discharged well on February 12, 1896, the only surgical procedures having been antiseptic dressings and skin graft.

Second admission. Thirty years later, December 2, 1925, patient was again admitted (W. S. No. 273376), giving a history that his foot never had healed entirely since his accident, and that 5 years after he left the hospital it began discharging pieces of dead bone, with constant "festering." Examination showed a proliferating ulcerated growth occupying the instep and most of the plantar surface of the right foot (Fig. 8). A clinical diagnosis of carcinoma was made. A few days later amputation of the right lower leg was done by Dr. J. C. White, 3 weeks after which he was walking about on crutches and feeling very well. Pathological report showed squamous cell carcinoma, grade I. December 4, 1928, the patient was seen in the tumor clinic. There was no sign of recurrence.

In the 5 other cases found in the records of this hospital, the diagnosis and treatment were slightly different in each case, in 2 cases biopsy or excision being resorted to in order to establish the diagnosis, and in 2 other cases, in spite of a positive diagnosis of cancer, amputation not being considered necessary. In Case 11, incision and drainage, and failure to heal led to a secondary operation, when pathological fracture occurred, followed later by amputation.

CASE 7. G. A. D., a married white man of 42 years (W. S. No. 130621) entered the hospital January 16, 1903, because of a discharging sinus in the right lower leg, dating from an operation for osteomyelitis when he was 10 years old. There had been many exacerbations, but about 3 months before admission the pain became very intense, he had to give up work, and he noticed a small growth appearing at the old sinus. Examination showed a diffuse tender enlargement of the ankle with three discharging sinuses just above it, and a round, ulcerating growth discharging foul material around the upper sinus. Biopsy of this ulcer showed it to be an epithelioma.

Amputation of the leg through the femoral condyles was performed by Dr. J. C. Warren the day after admission, after which the patient made a satisfactory though somewhat stormy recovery.

CASE 8. *First admission.* T. P. C., a widower of 53 years (E. S. No. 133503) entered March 19, 1903, because of a sinus of the left lower leg, discharging pus and pieces of bone off and on since the patient was 2 years old. Examination showed on the left lower leg toward the inner side and midway between

Fig. 7, left. Appearance of leg on admission. Diagnosis of carcinoma in osteomyelitis evident on history and inspection. Case 4.

Fig. 8. Two views, showing extensive malignant growth of instep. Case 6.

the tibial tubercle and the malleoli, an irregular sloughing area surrounded by granulations. There was a moderate discharge coming from the tibia, which was exposed and considerably thickened. Carcinoma was suspected. Operation was performed by Dr. C. A. Porter 2 days after admission, the area widely excised, and the bone chiselled away. Microscopic examination showed epithelioma. About 2 weeks later the patient was discharged with a clean granulating wound.

Second admission. Six weeks after discharge, the patient returned because of a bright erythema about the inner side of the granulating wound on the leg, suggesting erysipelas. After 2 weeks in the hospital, the erythema subsided and the patient was discharged, there still being present a sluggish granulating area.

Third admission. Two months later he was again admitted for treatment of the ulcer of his left lower leg. A low thigh amputation was performed by Dr. C. L. Scudder, microscopic examination again showing epithelioma. Convalescence was uneventful. Eight years later he was seen and found to have had no recurrence.

In the 2 following cases, a local removal of the growth without amputation was considered sufficient.

CASE 9. W. H. L., a married man of 46 years (E. S. No. 283779) entered the hospital on May 24, 1927, with a chief complaint of abscess of the right

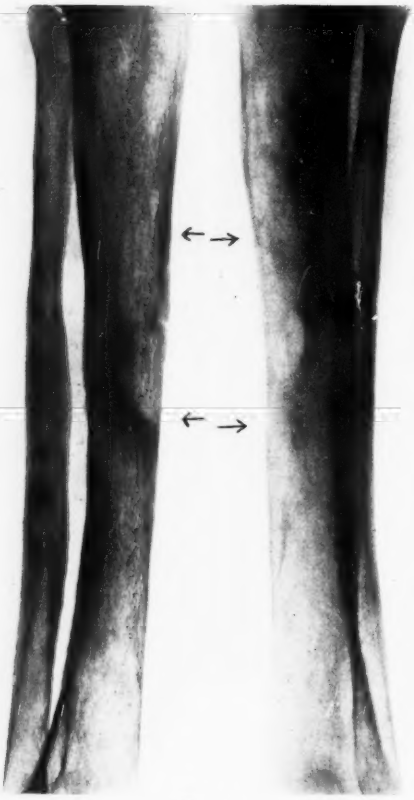

Fig. 9.

Fig. 10.

Fig. 9. Anteroposterior and lateral X-rays of tibia, showing only extensive osteomyelitis. The carcinomatous portion is indicated between the arrows. Case 9.

Fig. 10. X-ray pictures taken about 6 weeks after operation, showing amount of bone removed at operation. Case 9.

shin. He had been operated upon 5 months before at a local hospital, for an ulcer of the leg which had been discharging pus for an unstated period of time. Following operation the lesion, instead of healing, grew progressively worse and the patient lost 11 pounds in weight. Physical examination showed at the lower third of the right tibia anteriorly a fungating, irregular lesion with a sloughing center and raised borders, surrounded by a blue indurated skin, the center crater being about 4 centimeters in diameter and apparently involving the bone. The X-ray (Fig. 9) was reported as follows: "The bones of the tibia are increased in size and irregular in shape. The cortex is thin and shows marked variation in density. In the midportion is an irregular area of diminished density with a line running through it, suggesting a fracture line. Such an appearance could be due to old osteomyelitis. No evidence of activity."

Operation was performed by Dr. E. M. Daland 2 days after admission, the pre-operative diagnosis being carcinoma in scar of osteomyelitis. The incisions were carried around the growth and down to bone, and showed the carcinoma involving bone. The carcinomatous bone was chiselled away and an area of chronic osteomyelitis was drained.

Pathological examination showed a large ragged ulcer 6 centimeters in greatest diameter, with fragments of bone adherent to its under surface, squamous cell carcinoma, group II.

X-rays taken about 6 weeks after operation (Fig. 10) were reported as follows: "The patient has apparently been operated on since the last observation. Apparent removal of a portion of the bone in the anterior and medial portion of the tibia. The entire tibia shows osteoporosis and some thickening of the cortex; may be due to old inflammatory process."

Fig. 11. Fig. 12.

Fig. 11. Pre-operative X-ray pictures. The irregular worm-eaten area indicated between the arrows is typical of malignancy. Case 11.

Fig. 12. X-ray pictures taken at the time of the pathological fracture, showing progression of the lesion. Case 11.

The wound healed well with Dakin's dressings and a skin graft was applied a month later, the patient being discharged about 3 weeks thereafter.

The patient's condition was followed in the tumor clinic, where 3 years later there was no evidence of recurrence either clinically or by X-ray. The wound had remained well healed for 1½ years and the patient had had complete use of the leg.

Case 10. A. C. P., a single white male of 58 years (W. S. No. 226319) entered the hospital November 5, 1918, because of a sore left heel of 12 years' duration, which would nearly heal, but would then break down and cause pain and lameness necessitating the use of crutches. Physical examination showed a granulating, sluggish, ulcerated area on the left heel about 2 centimeters in diameter. X-ray examination showed a marked irregularity and roughening on the under surface of the os calcis. There was also considerable increased density in that region. The appearance was that of chronic osteomyelitis, without evidence of malignancy. Operation was performed a few days later, by Dr. C. C. Simmons, the growth being excised and a skin flap swung over the heel from the outer side of the foot. Microscopic examination showed the corium invaded by an interlacing network of atypical epithelial cells, with abundant small round cell infiltration-carcinoma. Seven weeks later, after two skin grafts, the patient was discharged relieved.

In the following case, carcinoma was not definitely diagnosed until a pathological fracture occurred on the operating table, at which time both the X-ray and microscopic findings showed carcinoma.

Case 11. L. B., a single white male of 34 years (W. S. No. 278625) entered the hospital on September 10, 1926, the chief complaint being pain in the right leg, dating back 30 years to a painful swelling

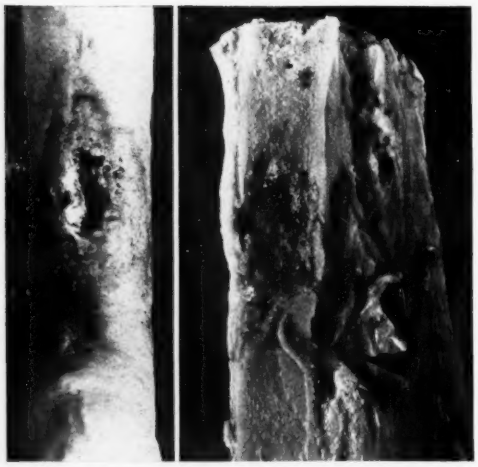

Fig. 13, left. Appearance of sinus on admission. Case 12.
Fig. 14. Photograph of longitudinal section, showing that the lesion has progressed almost completely through the bone. Case 12.

of the leg which required operation when the patient was only 4 years old. Seven operations were performed in the next 16 years, with a discharging sinus ever since the last operation. Examination showed a large area of broken skin 5 centimeters above the right ankle in which necrotic bone was plainly evident. X-ray (Fig. 11) taken September 13, was reported as atypical, and no positive conclusions were drawn from it.

Operation was performed 4 days after admission, soft necrotic bone with a foul odor being chiselled and curetted away. Three weeks later it was noted that the sinus was not cleaning up and the necrotic bone seemed to be extending. Accordingly biopsy was performed on October 7, during which operation the patient sustained a pathological fracture at the point of the diseased bone. Microscopic examination of the tissue showed epidermoid carcinoma. X-ray examination (Fig. 12) at this time was reported to be characteristic of malignancy. Amputation just below the knee was therefore decided upon and carried out a few days later by Dr. J. W. Spellman, the patient making an uneventful recovery.

Eight months later he was examined in the Out-Patient Department and was found to have no recurrence. His condition was followed thereafter in the tumor clinic where, on the last examination August 6, 1929, there was no evidence of recurrence of the disease, though there was apparently a neuroma in the amputation stump. A letter received in June, 1930, indicated no change in the patient's condition.

Since the first preparation of this paper there has occurred another similar case which is summarized herewith. In some respects it is the most interesting case of all, particularly in regard to diagnosis, for although we were alert clinically to the likelihood of carcinoma, it was difficult by X-ray and even by biopsy to establish a positive diagnosis.

CASE 12. *First admission.* H. L. F., a boy of 6 years (W. S. Vol. 147, p. 189) entered the hospital on October 5, 1871, because of swelling of the left leg of 1 year's duration. Inflammation had increased without known cause during the past year, until constitutional symptoms developed. Sinuses at length became established over the tibia, through which dead bone appeared. Examination showed some limitation of motion of the knee joint and one of the sinuses connected with the ankle joint. Two days after admission operation was performed by Dr. R. M. Hodges. "A long incision was made over the crest of the tibia; nearly the whole of the shaft and a portion of the lower epiphysis were found necrosed, and were removed after gouging out the anterior wall of the new bone." The patient made an uneventful convalescence and was discharged well only 6 days after the operation. Diagnosis: necrosis of bone.

Second admission. Fifty-nine years later, when he was 65 years of age, he was again admitted to the hospital (E. S. No. 306925) because of pain in the left lower leg and a discharging sinus. Since his previous admission there had been occasional periods when a small sinus had opened, with slight discharge and the appearance of small pieces of bone. On the whole, however, the leg had troubled him very little until 6 months ago, when he was struck on the left shin, after which a sinus developed and kept on increasing in size. Recently there had been so much pain and foul discharge that his leg had been of little use to him. Examination on admission (Fig. 13) showed a sinus 8 centimeters long and about 2 centimeters deep in the anterior lower third of the left tibia, discharging a very foul watery material.

Because of the very long history and extremely foul appearance of the lesion, carcinoma in old osteomyelitis was at once suspected.

X-ray (Fig. 15) showed some of the characteristics of cancer in bone, but it was not certain whether the recent bone destruction was due to active osteomyelitis or carcinoma.

The first biopsy, done soon after admission, showed considerable proliferation of the epithelium, which was not considered sufficient to justify a diagnosis of carcinoma. The second biopsy, however, showed epidermoid carcinoma, grade I.

In view of the extent of bone involvement both clinically and by X-ray, a Gritti-Stokes amputation was decided upon, and performed by Dr. R. H. Wallace, following which the patient made an uneventful convalescence.

The appearance of the sinus in longitudinal section is shown in the photograph (Fig. 14). There is so

little normal bone remaining near the lesion that it is remarkable that there had been no pathological fracture.

Carcinoma is an extremely rare complication of osteomyelitis, only 12 cases having been found out of 2,400 cases of osteomyelitis treated in the wards of the Massachusetts General Hospital. Although little has been written about it recently, the lesion is very well defined and important to recognize. In a large clinic the possibility of its occurrence in any case of long-standing osteomyelitis should be borne in mind.

In our experience the disease has been confined entirely to males, owing probably to the fact that osteomyelitis is more common in the male sex. The tibia was involved in 8 cases, the foot in 3, and the femur in 1. This does not correspond exactly with the figures of this hospital for the location of osteomyelitis, i.e., out of the 2,400 cases of osteomyelitis, the largest number were in the femur (616), and a much smaller number in the foot (156). The tibia, however, as is well known, is a very common site for osteomyelitis, and in this location there were 586 cases, 8 of which developed cancer. No cases of cancer were found developing in osteomyelitis of the jaw (267), humerus (150), radius and ulna (106), hand (119), or other scattered locations. Scudder, however, says that "carcinoma sometimes follows in the sinus or edges of old fistulous tracts about the jaws." All of our cases of cancer of the jaw were carefully reviewed and none could be surely traced to an osteomyelitis as their origin. Two cases of cancer of the upper jaw gave histories of chronically infected bone, but pointed rather more to an origin in the antrum than to osteomyelitis. It seems reasonable to explain this by supposing first, that better circulation of the face and upper extremities tends to more rapid healing in chronic osteomyelitis in these localities, and second, that many patients would not tolerate foul sinuses on the face or upper extremity for a long enough time to permit the development of cancer. In the leg, however, the circulation is often poor, and patients are apparently willing to neglect very foul lesions for many years. In one case (Case 4) osteomyelitis had been present for 64 years, with alternate healing and breaking down of the sinus, and discharge of fragments of necrotic bone; in fact, the majority of cases give a history of over 30 years' duration.

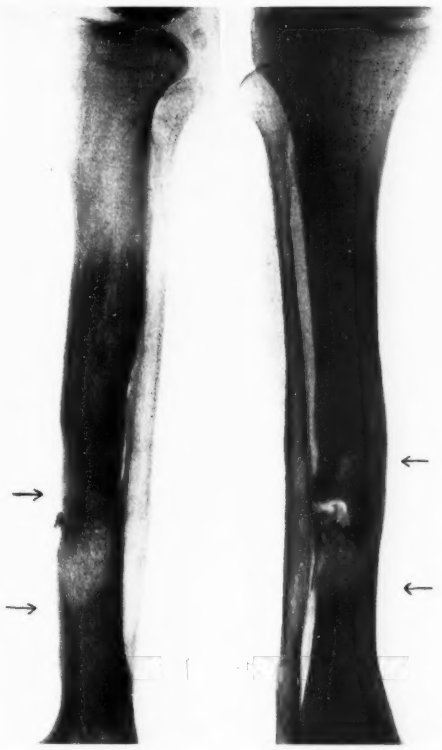

Fig. 15. Area indicated between arrows shows the site of carcinoma. The roentgenogram shows some of the characteristics of cancer in bone. Note the extreme calcification of the artery. Case 12.

The history and course of the disease in a typical case is somewhat as follows:

A man of middle life or beyond enters the hospital because of foul ulcers or sinuses, generally of the lower leg, but sometimes of the thigh or foot. In about half the cases, pain is a prominent symptom. Not infrequently there is a history of trauma preceding the onset of the osteomyelitis. Usually surrounding the fistulous opening there is a fairly definite cauliflower mass which leads at once to the diagnosis of carcinoma. In some cases, however, there is no external evidence of malignant disease, or in others there may be a slight epithelial overgrowth at the margin of the sinus opening.

In all suspicious cases a biopsy should be done, and if carcinoma is found there is very good likelihood that the disease has spread inward along the tract and is involving the bone. Where there is no external evidence of malignancy, it may be impossible to make the diagnosis until the osteomyelitis cavity is explored, at which time either the gross appearance or microscopic examination of frozen sections will lead to the correct diagnosis.

X-ray examination, of course, is made in all cases before operation, but it has not been possible in the few cases studied by X-ray since the introduction of good apparatus, to make the diagnosis of carcinoma in osteomyelitis by X-ray alone. The series presented, with X-ray photographs in 4 cases gives a very good idea of the variation in the X-ray findings. Case 1 (Figs. 5 and 6), for example, showed by X-ray very similar lesions of both femur and tibia, supposedly both due to osteomyelitis, and yet pathologically the tibia showed only osteomyelitis while the femur showed carcinoma as well. On reviewing these X-ray films very carefully there are found some areas in the femur which might make one suspect carcinoma. Similarly in Case 12 (Fig. 15), the areas of bone destruction might have been due to active osteomyelitis or to carcinoma. In Case 9, however (Figs. 9 and 10), the X-ray gives no clue whatever as to the presence of carcinoma. Finally, in Case 11 (Figs. 11 and 12), the X-ray appearance is typical of carcinoma, and with some knowledge of the patient from a clinical standpoint, the roentgenologist should be willing to report definitely carcinoma in osteomyelitis.

The treatment in 9 of these 11 cases was amputation; in the 2 others, radical excision of the growth locally. As it may be impossible to tell to what extent the carcinoma has invaded the bone in a given case, it seems wise to recommend amputation in most cases. If, however, the X-ray film shows very little bone destruction, and the carcinoma seems to be merely lining the wall of the cavity, a thorough local excision may suffice, for this type of cancer usually progresses slowly.

The pathologist may demonstrate that the carcinoma is very superficial or (as in Case 1) that it has invaded the bone to a depth of 1 or 2 inches. In any case it is always of the epidermoid variety, indicating that it arises from the epithelium surrounding the sinus, and grows inwardly along the wall of the fistulous tract. It seems probable that the chronic irritation to the epithelium from constantly discharging infectious material plays a part in the etiology of this type of carcinoma.

As the disease is ordinarily of the slowly growing epidermoid variety, and usually without metastasis in the groin, the prognosis under proper treatment is favorable.

CONCLUSIONS

Carcinoma is a rare complication of very long standing osteomyelitis, occurring more often in the tibia than in any other bone.

The diagnosis may be very easy when the growth is superficial or very difficult when deep-seated; in some of the latter cases a diagnosis can be established only by biopsy, or rarely, perhaps, by X-ray examination.

The treatment should be first, prophylactic, in not permitting osteomyelitis sinus to remain open indefinitely; and second, curative, by amputation in most cases.

The prognosis is generally favorable, the condition being of slow development and usually of low malignancy.

NOTE.—The author wishes to express his appreciation to Drs. E. P. Richardson, G. W. Holmes, and J. I. Bradley for their assistance and suggestions in the preparation of this paper.

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EXPERIMENTAL REGENERATION OF THE THYROID GLAND

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IN a previous paper, the writer called attention to changes in the normal thyroid gland of the dog, one of which changes is of destructive (Fig. 1), the other of reconstructive character (Figs. 1 and 2). The fact was established that during normal conditions the organ shows a continuous regeneration in order to replace exhausted or destroyed tissue; the replacement seems to keep pace with the destruction. Consequently, it may be supposed that the process of regeneration will be much more pronounced in the organ in which the amount of normal tissue is suddenly decreased, as for instance by the operative removal of a part of the tissue. The physiological destruction and regeneration sometimes proceed very slowly and in such small areas that these processes may easily escape the notice of the observer, just as the steady regeneration of the blood or of the superficial layers of the skin remains inconspicuous. For purposes of comparison reference may be made to the myelolymphatic system, to the stratum germinativum, to the periosteum, and to the intima as the respective centers of new formation of blood, skin, bone, and blood vessels. Other analogous examples could be mentioned. All such centers show an increased activity in conditions causing an increased destruction of the specific tissue. Centers of regeneration which may be inconspicuous in the normal course of an organ will become more distinct during the increased necessity for restoring the loss of a large amount of its specific tissue. In view of this fact the study of regeneration in the thyroid gland leads to the consideration of two questions: (1) whether restoration of thyroid tissue is possible due to the existence of regeneration centers, and (2) whether the groups of small follicles pointed out by the author as the regeneration centers of the normal gland are also the regeneration centers of the gland after a part of the tissue has been removed.

The possibility of regeneration of the thyroid gland has been considered by other authors who agree that such activity takes place in the thyroid gland under experimental conditions. The papers of Huerthle (1894), Crawford and Hartley (1925), Else, Grow, and Lemery (1926), Marine (1926), and Else (1927) supply evidence of the regeneration of thyroid tissue. The writer's experiments confirm their conclusions. These investigators, however, did not compare, it seems, the conditions in the normal gland with those active in the regenerating gland.

In a group of dogs the ventral half of both lobes of the thyroid gland was removed and studied as described in the writer's previous paper. The dogs were killed after different intervals following the operation, and the rest of the thyroid tissue left inside was examined.

The findings in some of the cases are computed in Table I. The number of crosses indicates the relative amount of destruction and regeneration of follicles; the table shows that in the normal tissue regeneration generally keeps step with destruction. The normal balance between the destructive and the regenerative processes in those portions of the gland left in place is modified not only by increased regeneration but also by decreased destruction of the thyroid tissue. The regeneration was followed over a period longer than 5 months.

TABLE I.—FINDINGS. THE RELATIVE AMOUNT OF DESTRUCTION AND REGENERATION IS INDICATED BY CROSSES.

No.	Days elapsed since operation	Normal thyroid removed by operation		Regenerating thyroid	
		Destruction	Regeneration	Destruction	Regeneration
4627	59	++++	+	o	++++
4396	61	+++	+	+	++++
4573*	87	+++	++	o	++++
4467	129	+++	+++	++++	+
4364	157	+++	+++	+	+++
4332	164	+++	+++	+	+++

*This case was used also for the illustrations of this paper.

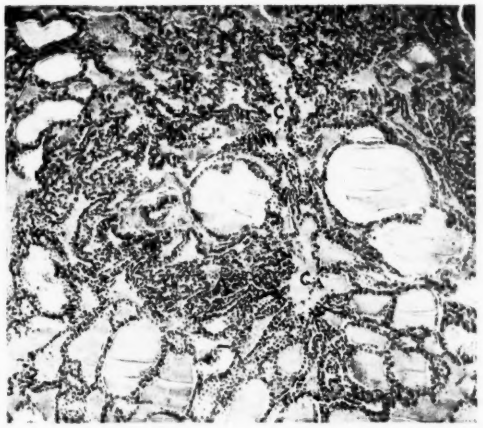

Fig. 1. Photomicrograph of a section through the normal thyroid of a dog (approximately × 90), showing destruction of follicles. *A*, Collapsed follicles; *B*, disintegrated follicles, mingled with colloid; *C*, space filled with colloid resulting from the fusion of several follicles. In the left lower corner a "normal" area.

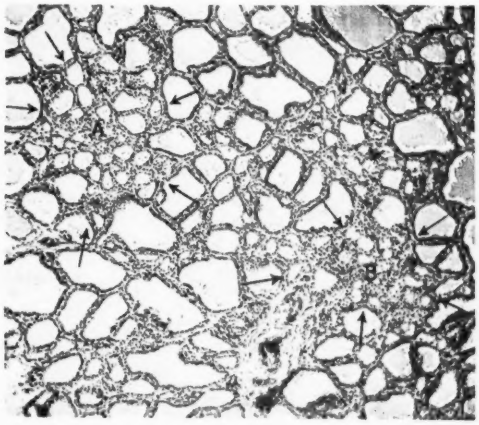

Fig. 2. Photomicrograph of a section through the normal gland of a dog (approximately × 90), showing the regeneration of thyroid tissue probably from persisting embryonic tissue, *A*, and from disintegrated areas, *B*, already containing few new follicles.

All the glandular tissue left in place shows typical changes when studied some time after the operation. The amount of destruction of follicles is very much reduced and cannot be found in as many localities as in the normal uninjured organ. It seems that the gland protects itself against further destruction.

However the table shows one case, No. 4467, which does not conform to the results of the other cases. It is possible—as the study of the sections suggests—that a greater quantity of thyroid tissue was removed in this dog than in the other dogs. May it be that the loss of such tissue was too great to permit a restoration commensurate with the increased demand of colloid by the body—if the view be true that colloid is released from follicles only by their destruction?

In any normal uninjured thyroid gland it was found that the wall of a follicle is not a permanent structure. In time its cells lose their contiguity and become intermingled with colloid. Some of them disintegrate and fuse with the colloid, while others, especially those at the periphery of such dissociated follicles, keep their normal appearance and seem to continue their function. The colloid liberated by the destruction of follicles is probably resorbed by the lymph vessels and carried away. In other places of the normal thyroid gland, there are regions which consist not of follicles with typical lumen and cellular arrangement, but of cell groups arranged as solid masses. In such areas small distinct groups of cells are observed which represent the early stages in the new formation of follicles. The development of new follicles from such groups of resting cells compensates

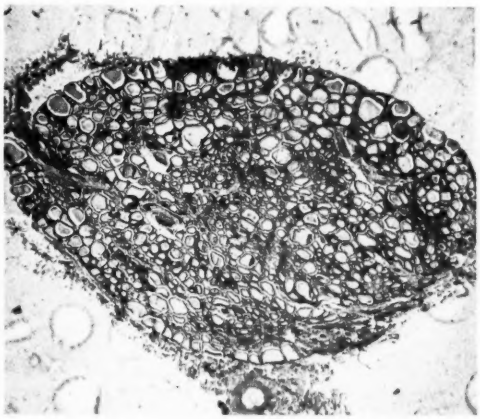

Fig. 3. Photomicrograph of a section through the regenerating thyroid gland of a dog; 87 days after operation (×15). Small follicles are characteristic of the regenerating areas; large follicles already present before operation.

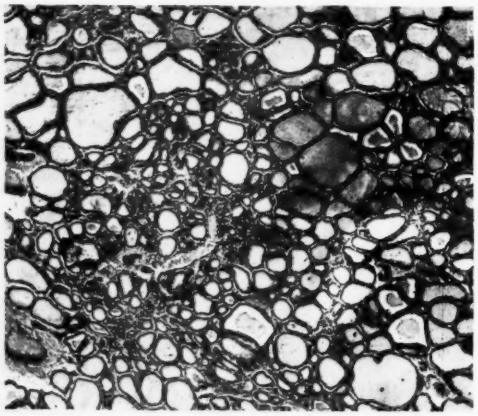

Fig. 4. Photomicrograph of a section through the regenerating thyroid gland of a dog; 87 days after operation (×42). The regenerating area shows not only small (new) follicles but also interfollicular cell groups from which they developed.

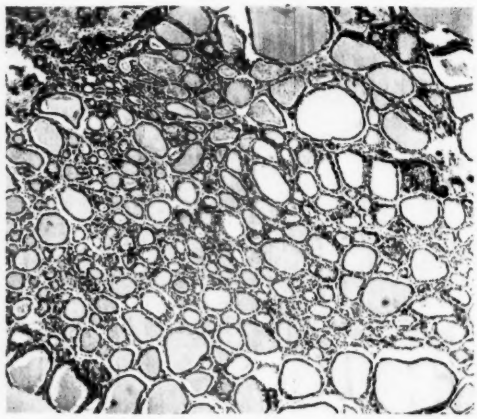

Fig. 5. Photomicrograph of a section through the regenerating thyroid gland of a dog; 87 days after operation (×51). Interfollicular cell groups and new follicles of different size (age) are easily distinguished from the follicles already existing before the operation.

the loss or destruction of defunct follicles. Newly formed follicles are derived from one of two sources, either from persisting embryonic cell masses or from cells which remain after the destruction of follicles.

The regenerating gland—restricting this name to the tissue left inside the body—shows a changed structure, represented in Figure 3, in comparison with the normal gland (Fig. 2) which had been removed at operation. The section contains many scattered areas of small follicles varying in size. The large follicles possess the size of those in the normal gland. Comparing this section (Fig. 3) with one of a normal gland, the observer finds it easy to distinguish the part of the gland removed at operation from the part

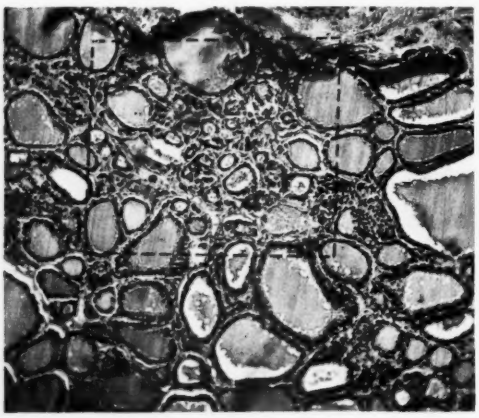

Fig. 6. Photomicrograph of a section through the regenerating thyroid gland of a dog; 87 days after operation (×90). Area indicated by dotted line represents regenerating area illustrated by higher magnification in Figure 7.

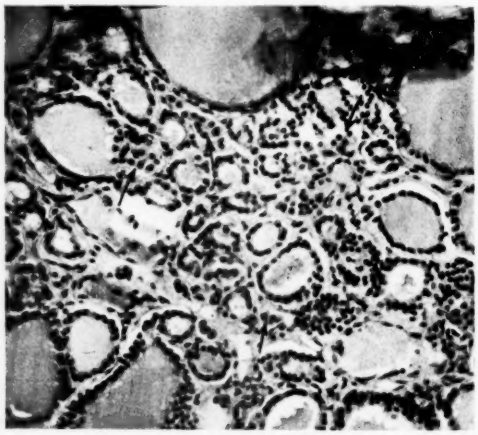

Fig. 7. Photomicrograph of a section through the regenerating gland of a dog; 87 days after operation (×177). Between the regenerating follicles many cells of the large type, described in the text, are indicated by arrows.

regenerating. The areas of regeneration are distributed irregularly throughout the whole section. The difference between the regenerating and the normal-sized follicles—remaining from the time before the operation—is illustrated in Figure 4 which, because of its larger magnification, shows these features better than does Figure 3. The fields of regeneration contain not only follicles of small size but also solid cell groups typifying reserve tissue able to reproduce new follicles as needed. Some similarity exists between such an area, as shown in Figure 4, and a gland during the embryonic period. Figure 5 portrays a part of a section through a region in which active regeneration was taking place. Only a few solid cell groups are left. Typically the colloid fills a young follicle completely and is not retracted from the cells. The cells themselves are cuboidal and increase in number with the growth of the follicle.

Cells, larger in size than commonly and containing a homogenous protoplasm, as described previously by the author, are also found in the regenerating thyroid gland. The region indicated in Figure 6 is seen under higher power in Figure 7, and is characterized by the presence of these cells. It is difficult to express a definite opinion concerning the significance of these cells and their relationship to the follicular cells. Further investigations may clear up this point.

SUMMARY AND CONCLUSIONS

It was shown by experiment that the thyroid gland is able to replace by regeneration a loss of thyroid tissue, an observation which is illustrated by photomicrographs of sections of regenerating glands.

The regenerating power must be assumed to be always potentially present in certain areas of the normal gland, otherwise regeneration would not be possible. These areas represent the points from which the normal gland restores the loss of secreting tissue caused by continuous destruction of thyroid follicles.

It was also shown that both in the normal and the regenerating thyroid there occur large cells of polyhedral or spherical shape with homogenous protoplasm and large nucleus which are located outside the follicles and are entirely different from the cuboidal cells of the follicle.

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COLLATERAL RESPIRATION IN THE LUNG

Rôle in Bronchial Obstruction to Prevent Atelectasis and to Restore Patency[1]

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RECENT investigation of ours, reported elsewhere (3, 4), has shown that the branches of the bronchial tree are interconnected abundantly at the periphery in such manner as to permit gases, thin fluids, and particulate matter to pass from one to the other. The connection lies between the fine arborization throughout all parts of a single lobe, and it is lacking between lobes; that is, it is interlobular and not interlobar.

The present paper deals with the relation of this mechanism to pulmonary function. The experimental findings which are to be reported indicate that it relates especially to bronchial obstruction. Thus, after blockage of one branch or portion of branches in the bronchial tree of a lobe, the corresponding lobule or group of lobules of lung parenchyma is not necessarily isolated and may continue to breathe by means of the peripheral intercommunications with adjacent unobstructed lobules. In this way, the air content of the parenchyma is maintained, atelectasis is prevented, and necessary assistance is rendered to the broncho-eliminative functions in expelling the obstruction. We have termed this function collateral respiration by analogy of principle and economic significance to the collateral circulation of the blood vascular system.

In introduction, those published observations will be reviewed which indicate the existence of interbronchial communication and are necessary to an understanding of its nature; and then collateral respiration and the parts that it plays in pulmonary function will

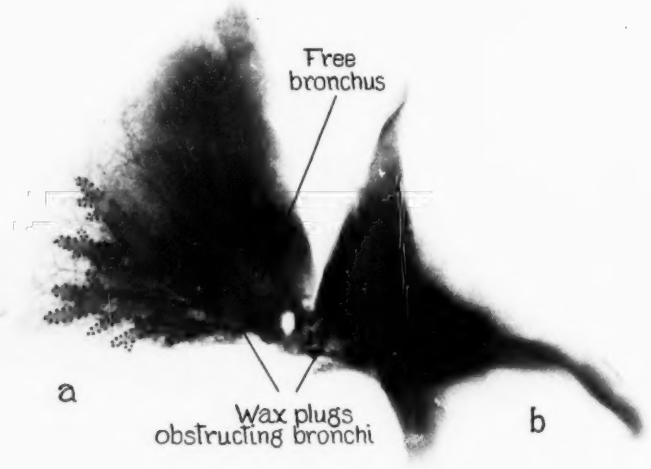

Fig. 1. Roentgenogram of two lobes of dog's lungs with bronchial obstruction lasting 3 days. *a*, Lobular obstruction; parenchyma quite air-containing. *b*, Lobar obstruction; atelectasis.

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be described. Each phase of the subject, in turn, will first be explained and then illustrated with protocols and other experimental data. All observations presented have been obtained repeatedly, but duplication is to be omitted.

INTERBRONCHIAL COMMUNICATION

Intercommunication between adjacent subdivisions of the airways of the lung was demonstrated most simply by securing a pulmonary lobe of a sufficiently large animal and blowing gently into one bronchial branch. The air, after entering and partially inflating the corresponding lobule of the parenchyma, escaped from the free bronchi.

Experiment 1. A dog's lungs were obtained immediately after sacrifice and one lobe was removed for testing, care being taken in separating it from the others to avoid injury to the parenchyma. Its stem bronchus was then dissected free as far as the first bifurcation and cut off, and into each of the two branches was tied a cannula. One cannula was connected to a source of air current, and the second was extended to a dish of water where its tip was submerged. A gentle current of air was then started and the lobule supplied by the first cannula was gradually inflated. At a time when inflation was nearly complete and without noticeable inflation of other parts of the lobe, air began to bubble from the second cannula. The escape was free. It continued with the injection and accounted entirely for the quantity of air injected. By limiting the rate somewhat, the injection could be maintained indefinitely without there resulting complete inflation of the first lobule or any loss of air from the pleural surface. Next, the second cannula was closed to retain the air. The remainder of the lobe then began to inflate, and inflation progressed in all parts simultaneously, precisely as in the first portion. Throughout the process up to full distention, appearances of inflation by radial progression from the boundaries of the first lobule were absent, as likewise was interstitial emphysema or any other evidence of rupture.

This experiment has been repeated with the same results with specimens from man, dog, cat, and rabbit. In the calf and pig, however, there was found not the slightest interpassage of air, even when the pressure of injection was elevated enormously and leakage from the pleural surface and interstitial emphysema were produced. Moreover, in all species examined, interpassage failed to occur from one pulmonary lobe to another, except in certain specimens of man and rabbit; and here pressures too high for any physiological significance had to be used for its accomplishment.

The test was repeated with the intact lungs of living dogs and interbronchial communication was demonstrated—interlobular but not interlobar in type.

Experiment 2. A dog was anæsthetized and tracheotomized. A long metal cannula was passed into the trachea and carried to the bronchi on the right side. The cannula was of such design (6) that its end could be forcefully dilated after insertion to secure it in the bronchial lumen with air-tight junction; and it was thus secured in one bronchial branch of the right lower lobe. A current of air was then passed into the cannula with pressure no greater than 1 centimeter of water, and it was found that this could be maintained indefinitely and hundreds of cubic centimeters could be injected without leaving the intrapulmonary pressures increased. Likewise, it was found that air could be sucked from the cannula continuously and with equally slight force in unlimited quantities without leaving depression of the intrapulmonary pressures. When, however, the cannula was loosened, withdrawn somewhat and resecured so as to fix it in the primary bronchus supplying all parts of the right lower and accessory lobes, the results were quite different. Air could be injected into or aspirated from the lung in quantities limited obviously to the capacity of the two lobes, and such displacements left marked and persistent changes in the intrapulmonary pressures even when no more than a few cubic centimeters of air were displaced. The dog was sacrificed and the position of the cannula verified. Its junction with the bronchus was tested for security and found to resist vigorous pull as well as very high air pressure and suction.

Certain inferences were drawn from the data concerning the site and mode of interbronchial communication as follows:

The observation in experiment 1 that passage of air from branch to branch of the bronchial tree was obtained only when the parenchyma was somewhat inflated points to the peripheral airways as the site of transfer. The transfer seems not to depend upon artifactious channels resulting from overdistention and rupture of the minute airways of one lobule into those of the other for three reasons, namely: extremely low air pressures were used (in experiment 1, insufficient to inflate the parenchyma completely, and, experiment 2, measured at 1 centimeter water or less), a radial pattern of dissemination and emphysema were absent, and the transfer occurred

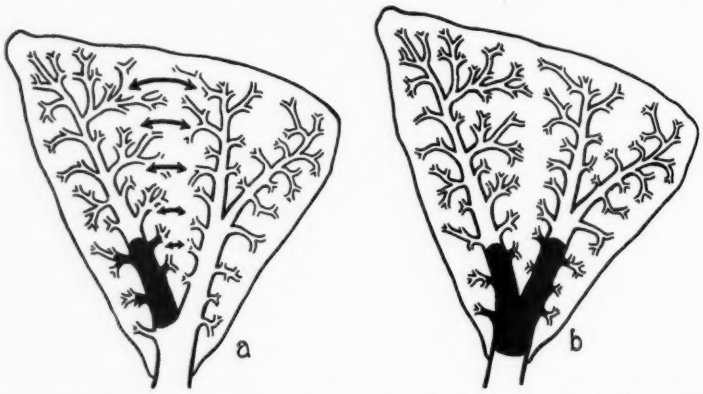

Fig. 2. Diagrams of bronchial trees of two lobes, showing *a* lobular, *b* lobar forms of obstruction, and arrows paths of collateral respiration.

spontaneously in quiet breathing (experiment 3). The appearances of intercommunication, as described, were explained readily by assuming that the air diffused through the tissue membranes separating the peripheral airways of adjacent pulmonary lobules. It was found, however, that India ink also accomplished the passage, and this pointed to the presence of anatomical openings. These openings may be the pores known to occur in the alveolar walls and believed by some (2) to exist normally. We have assumed that both diffusion and anatomical continuity operate as far as the transfer of gases was concerned. It seemed likely, as well, that the absence of air transfer in calf and pig between the main branches of the bronchial tree of the individual lobe and, in all species, between the airways of two adjacent lobes was due to their separation by connective tissue septa. Indeed, these septa were plainly evident. The lung lobes of calf and pig showed the pleural surfaces divided into patches by pronounced septa, and the lobules composing the patches could be readily split apart by blunt dissection. Such exaggeration of the division into respiratory units, except between the lobes, was not seen in the other species.

COLLATERAL RESPIRATION

Experimental results now at hand prove that collateral respiration may be instituted spontaneously and maintained indefinitely after bronchial obstruction in the living animal. This is shown by direct detection and measurement of the transfer of respiratory gases (alveolar air) to and from a pulmonary lobule, the bronchus of which is occluded centrally. The amount of the respiratory displacement is found to be appreciably large, perhaps even normal, for the portion of lung concerned. On the other hand, no such transfer occurs following obstruction of the stem bronchus of one or more entire lobes.

Experiment 3. A dog was anæsthetized and tracheotomized. One bronchial branch of the right lower lobe was cannulated as in experiment 2. The cannula was then connected by rubber tubing to a glass nozzle and the tip of this was submerged in water. This formed a valve permitting the cannulated lobule to expire, but not to inspire, by way of its bronchus. Air bubbled freely from the nozzle at each expiration, and this continued without cessation during a 1 hour period of observation, with the total discharge amounting to 1800 cubic centimeters. Then, the water-valve was rearranged so as to permit inspiration only, and in this way was allowed to operate for 1 hour. At each inspiration, air passed the valve and entered the cannula in quantity somewhat greater than that which escaped with each breath previously, and this continued unabated. Next, the cannula was loosened and resecured in the primary bronchus supplying the entire right lower and accessory lobes. The water-valve was arranged as at first, i.e., to permit expiration only. Now, after two or three breaths and escape of an amount of air approximating that of the tidal air, the discharge ceased and did not recur throughout the period (one-half hour) of observation. Again the valve was reversed and the capacity of the two

lobes to receive air was found to be similarly limited. The animal was sacrificed and the position and security of the cannula were proved.

Experiments of this sort, in which the dog is sacrificed and the lungs examined immediately after completion of a single phase of the procedure, show gross alteration in degree of inflation of the cannulated portion of lung only when the position of the cannula is lobar and the type of valve inspiratory. Here the parenchyma is found distinctly emphysematous.

Collateral respiration after blockage of the bronchus of a lobule may be prevented as result of loss of interconnection at the periphery of the lobule. This is found to occur in two ways. Thus, exudate and other materials may fill the fine peripheral air passages or alveoli which lie at the boundaries of the lobule and serve as pathways to the points of interconnection, as might occur in pulmonary inflammations; or there may take place what we believe to be a physiological shut-down of these airways. Belief in the latter circumstance is gathered from phenomena observed during the course of experiments of the type of experiment 3, where the animal has been allowed to lapse into deep surgical anæsthesia with shallow respirations for a period before institution of lobular bronchial obstruction. Collateral respiration may then fail to develop and the appearances are those of lobar obstruction and complete isolation of the cannulated part of the lung. A single deep breath on the part of the animal or artificial inflation of the lungs serves to establish collateral respiration, and that function then continues without further regard to the depth of breathing.

Experiment 4. A dog was anæsthetized with heavy doses of morphine and ether and was tracheotomized. It lay for 15 or 20 minutes breathing lightly and slowly, when the dilatable cannula was introduced and fixed in a bronchial branch of the right lower lobe. The cannula was provided with a valve permitting expiration only. An amount of air was discharged representing that of the tidal air, and then no more appeared. After a few minutes the anæsthesia was lightened to allow the animal to breathe more deeply. With the first deep breath, air began to escape at expiration and the discharge then continued as long as obstruction was maintained.

PREVENTION OF ATELECTASIS

Collateral respiration has the effect of preventing the formation of atelectasis after bronchial obstruction. Examples are at hand of blockage of bronchi applied for periods varying from 24 hours or less to 2 months without atelectasis, where the circumstances are such as to permit of collateral respiration. Thus, it proves to be the rule that a plug in the lobular position (Fig. 2a) with free interconnections at the periphery of the lobule is not followed by atelectasis; while a plug in the lobar position (Fig. 2b) may lead to atelectasis. In the former, the affected portion of lung is not isolated, and in the latter it is.

Experiment 5. A dog was deeply morphinized and a bronchoscope was introduced. Warm, soft wax was then carried into the stem bronchus of the accessory lobe and, also, into one branch of the bronchial tree of the right lower lobe. In each of these locations, the wax was pressed in and forced to follow and distend the bronchus and its principal arborizations. The wax soon hardened and formed a tightly fitting mold in the bronchial lumen, effectually obstructing it at all phases of respiration. The bronchoscope was withdrawn and the dog was then allowed to sleep off the effects of the morphine. After a period of 3 days it was sacrificed and autopsied. The accessory lobe (lobar obstruction) was found to be solidly atelectatic, while the right lower lobe (lobular obstruction) was perfectly normal in all parts as to degree of inflation (Fig. 1, a and b). Both plugs were firmly in place and proved airtight by test with high pressure.

The development of lobular atelectasis after obstruction of the lobular type depends upon closure of the interconnections at the periphery of the lobule and the absence of collateral respiration. These circumstances are produced frequently without intention in experiments with dogs anæsthetized continuously for several hours. Patches of atelectasis appear in unmanipulated parts of the lungs in the cortex, and the bronchi which lead directly to them are found to be blocked by accumulated secretion, although the obstruction may be limited to the arborizations and evade any but the most painstaking examination. The pattern of its distribution is often quite clearly such as to include the channels along the borders, as well as those leading directly to the areas of atelectasis. However, occulsion with secretion of the peripheral interconnec-

tions cannot always be so demonstrated and this is due in part, at least, to technical difficulty in determining patency of these minute passages. We suspect, also, that in some cases their closure is due not to obstructing secretion but to physiological shutdown developing during the prolonged period of anæsthesia.

RESTORATION OF BRONCHIAL PATENCY

In a systematic study of the aerodynamics of bronchial obstruction, to be reported in detail elsewhere, the results indicate that collateral respiration may give at times essential aid to the forces of broncho-elimination by maintaining a normal volume of air in the lung parenchyma. The action of cough depends directly upon this air. Moreover, only that portion of the air present in the lung after the inspiration that precedes the cough, which is immediately available for expiration, is of service in expelling material from the respiratory tract. We have termed this fraction the available air (5). Actual measurement of the forces exerted by cough to expel a body occluding a bronchus shows that they fail as soon as the available air is absorbed, and that this may take place within 30 minutes. In like manner, the expelling forces of ciliary and peristaltic activity and drainage by gravity probably also depend upon the presence of a normal content of air in the lung; for it is found that as absorption of air occurs after bronchial obstruction and the volume of air is reduced, the pressure in the bronchus distal to the point of obstruction falls progressively. This is explained by shrinkage of the lung within its resisting and elastic environs. The pressure very soon lies below that in the bronchus proximal to the obstructing body, and this relationship is maintained throughout all phases of respiration, no matter how great the effort in respiration may be; for both pressures arise alike from the action of the chest wall and diaphragm. Suction is thus developed (seen at −20 centimeters water with the attainment of atelectasis) on the distal side of the obstructing body, and this may be expected to act against broncho-elimination. Provision is made by the action of collateral respiration for both of these requirements of the broncho-eliminative functions, i.e., replenishment of the available air and prevention of suction in the occluded airways.

SUMMARY OF RESULTS

The principle of respiratory mechanics that has been described would appear to have a broad economic significance in the functioning of the lower respiratory tract. Considering the exudative tendency of the bronchial mucosa and the disposition of the lungs to transudation, it is likely that obstruction of the smaller air passages occurs frequently. The more minute bronchioles possess no ciliary and little, if any, peristaltic function to assist in elimination. The lumen of one of these is so small as to be filled over considerable length by no more than a droplet of exudate or secretion, and the result of such occlusion would be completely to isolate the corresponding u nit of respiratory ducts, atria, and alveoli, if there were no peripheral interconnections. Then, unless special expiratory effort were soon instituted to make use of the air available for expulsion, it would be lost by absorption. Inspiration, no matter how forceful, would not be able to introduce air past the column of fluid to replace the absorbed air. Atelectasis must soon develop, and this lobule of parenchyma must then remain functionless until the exudate undergoes removal by absorption. Under these circumstances, a night's sleep for an individual with slight bronchial catarrh would be expected to leave the lungs considerably, perhaps seriously, handicapped for respiratory space. Indeed, a bronchial tree made up of blindly terminating branches would be as inefficient as a blood vascular system consisting of end-vessels; even more so, since respiration operates by ebb and flow rather then by circulation of air, and since the forces impelling the air in quiet breathing are comparatively weak. However, as it is, since the bronchial tree has the function of collateral respiration, air is supplied to an obstructed lobule as long as the peripheral interconnections remain free and until such time as the block is eliminated by means of sufficiently forceful effort or by absorption.

The experiment (No. 5) which illustrates the effect of shallow breathing to prevent the institution of collateral respiration after bronchial obstruction calls to mind the clinical fact that prolonged shallow breathing in patients with excessive bronchial secretion is associated with special tendency to atelectasis, particularly in patients recovering from surgical operations. There it is known (1, 7) that the lungs are in a state of hypo-inflation, and we have reason to believe, therefore, that the effect is to shut down collateral respiration and mechanically to cripple the respiratory mechanism in the disposition of bronchial obstructions and the maintenance of function. Similarly, explanation is given for the effects of carbon dioxide inhalations or other means of deepening the respirations in preventing the occurrence of postoperative atelectasis. These maintain the normal degree of pulmonary inflation and thereby help to conserve the function of collateral respiration.

CONCLUSIONS

1. The branches of the bronchial tree in a single lobe of the lung intercommunicate at the periphery in such manner as to permit the transfer from one to another of gases, fluids, and particulate matter. The process of transfer is referable both to diffusion and to passage through minute openings, but this point requires further investigation. The airways of two neighboring lobes do not so communicate.

2. This bears economic significance to respiratory function after bronchial obstruction; for a lobule of lung with centrally obstructed bronchus may yet breathe satisfactorily by using the peripheral interconnections with adjacent free lobules. We term this function collateral respiration.

3. Collateral respiration plays two economic rôles in the lobular form of bronchial obstruction, namely, that of preventing the development of atelectasis, and that of rendering important assistance to the broncho-eliminative forces.

4. Collateral respiration may be excluded by closure of those airways along the margins of the obstructed lobule which have to do with the intercommunication. This may result from blockage with secretions or other materials or from shut-down during periods of shallow breathing. The latter circumstance is probably a factor in the pathogenesis of postoperative atelectasis.

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THE ORIGIN OF "ENDOMETRIOSIS" OF THE OVARY

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IN the last decade, few conditions have attracted so much attention or have been the subject of so much investigation as have the multiple perforating blood cysts of the ovary. Writings concerning these cysts have been limited almost entirely to the present century and the greatest interest has been evinced comparatively recently; nevertheless the volume of literature is astonishing. A number of hypotheses have been submitted, but none of these has proved completely satisfactory.

A study of "endometriosis" of the ovary has led the writer to conclusions which differ radically from most of those which have been reached by other investigators. These appear to be supported sufficiently both by personal observations and the descriptions of other writers; and they provide a simple explanation of the origin and many of the characteristics of the cysts. When this study was commenced, the writer was thoroughly imbued with the opinion that Sampson's hypothesis left little to be desired (1). It was only after a long study of the ovary itself that difficulties in its acceptance became manifest. Since the numerous hypotheses extant are not completely satisfactory, the evidence for this further suggestion is submitted.

HYPOTHESES OF ORIGIN

The hypotheses of origin of the multiple perforating blood cysts may be divided into three main groups:

1. Development from embryonal tissues: (a) wolffian body or duct, (b) the muellerian ducts.

2. Postembryonal development: (a) from the serosa, (b) from lymphatic endothelium.

3. Postembryonal displacement of endometrium: (a) by way of the fallopian tubes, (b) by way of the veins, (c) by way of the lymphatics.

These various suggestions have been considered so fully by many writers that but little discussion is necessary.

1. The development of tissue from hypothetical cell "rests" may be disregarded in the presence of more satisfactory suppositions.

2. The evidence for the development of multiple blood cysts from the serosa—in some cases—is very strong and it seems probable that some examples of the condition, e.g., in the umbilicus, are of this origin. In the case of the ovary, an origin from the surface epithelium (which corresponds with the serosa) is suggested by some observations but these do not explain the majority of the cases.

An origin from lymphatic endothelium is an important suggestion and will be referred to again.

3. In 1921, Sampson (4, 7) described these cysts in a most thorough manner and his work has been responsible for the remarkable popularity of their study. He postulated that they arose by the growth of pieces of endometrial tissue which had become transplanted on to the surface of the ovary, having been transported by way of the fallopian tubes. Later, he modified this view and described the passage of portions of endometrial tissue along the uterine veins to the ovary.

This work has resulted in the acceptance, by many gynecologists, of the idea that the cysts dealt with, are not only like endometrium but are truly endometrial.

In 1924, Halban added the modification of the passage of tissue by the lymphatics.

In order to explain the preponderance of the blood cysts in the ovary over those of the surrounding peritoneum, Sampson (6) regarded the ovarian growths as being the primary developments and the peritoneal cysts as arising from these, following their rupture. He postulated an affinity of the ovarian tissue for these endometrial implants, stating that the ovary acted as an "incubator" or "hotbed" for the pieces of endometrium during their early development.

This hypothesis which was proposed by Sampson has attracted the greatest attention. One cannot but admire the large amount of

energy and ingenuity which has been expended in the elaboration of this idea. The majority of those interested in the subject appear to have wholeheartedly accepted the explanation. There are, however, a number of difficulties to be overcome, and despite this, one observes writers regarding the suggestion as fact—or at least intermingling observation and suggestion so that the disentangling of description from hypothesis becomes extremely difficult.

Several important pathological principles must be resurrected before a true appreciation of the nature of the blood cysts can be obtained. They must, indeed, be disinterred from a mass of philosophical argument concerning, primarily, morphological resemblances, and, consequently, implantation of tissues, spread of viable tissue through the natural passages, spread through venous backwaters and concerning statistics of the frequency of the occurrence of blood cysts.

The striking feature of the evidence in favor of the implantation hypothesis is the large number of circumstantial observations (singly of little importance) and the complete absence of anything in the nature of direct proof.

The general laws which must be kept ever to the fore in pathological investigations fall into two main groups:

1. Certain principles have for their support a large mass of evidence accumulated during many generations and these should be applied to observations before the introduction of new or conjectural variations of these principles.

2. Pathological structures should be interpreted in terms of the physiological reactions and embryological character of the tissue in which or from which they arise.

For the explanation of endometrial implantation, certain unusual if not unique pathological processes have been invoked.

The implantation of presumably normal adult tissue into other organs of the body, where these implants assume an irritative character is surely a departure without precedent from accepted pathological teaching. Of course, precedent is unnecessary if the explanation is all-sufficing and if, therefore, no better suggestion may be made, but it is proposed to show that one other point of view, at least, should be considered before accepting this less probable origin. The necessity for the introduction of the idea of a "hot-bed" or "incubator" suggests immediately that some ordinary feature has been overlooked.

The passage of abnormal tissue along natural passages with subsequent implantation on a surface has been described on several occasions, though in but few examples can this explanation be regarded as satisfactory. Usually other mechanisms, e.g., passage of the tissue by the blood vessels or the lymphatics, afford a more probable explanation. All examples of transplantation of tissue (of doubtful viability) through the natural passages should be viewed with extreme caution.

Passage of tissue through the vessels from the uterus to the ovary is difficult of comprehension in the absence of emboli in the lungs, in the case of veins; or in the lymph nodes, in the case of the lymph vessels. In addition a retrograde spread from the uterine vessels into the ovarian veins or lymphatics must be postulated to explain the position of the cysts.

Pathological teaching with regard to the relationships of certain neoplasms to their parent tissues has been emphasized, of recent years, by the use of such terms as chorioma, folliculoma, thyoma, among many others. Any statement concerning the advisability of the use and multiplication of such terms is unnecessary, but the underlying principle is most important. When tissues, which will respond in a certain manner to abnormal stimuli, are present, it seems unnecessary and is indeed undesirable to postulate extraneous material until that of the involved organ has been thoroughly explored.

Any investigation into a disease of the ovary should be preceded by a thorough investigation of the embryology and physiology of that organ.

An axiom that has been overlooked is that morphological and even physiological similarity does not constitute identity. Too readily has it been accepted that the "endometrial" character of the epithelium of the

perforating chocolate cysts can be concluded with safety from morphological similarity, the presence of subepithelial stroma, the occurrence of hæmorrhage into and around the cysts, and the presence of decidual changes in epithelium and stroma during pregnancy.

This conclusion may be attacked from two different points of view:

1. The development of tissues apparently identical with a given type, may take place at a distance from the usual site of occurrence of the type tissue, without there being any question of transplantation. The development of squamous epithelium in a bronchus or of "gastric" glands in a gall bladder are excellent examples of the phenomenon. The importance of metaplasia is coming to be appreciated more and more of recent years. This viewpoint is accepted and used by the protagonists of the serosal hypothesis.

2. Other tissues, obviously not endometrial, may show the characteristics mentioned. Columnar epithelium indistinguishable by the methods in use from uterine epithelium occurs in ovarian cysts and tumors. A subepithelial stroma is common in many glandular neoplasms, not only in the ovary but in other parts of the body. Hæmorrhage occurs in cysts other than the "endometrial," e.g., the luteal cysts. Decidual changes may be found in the subepithelial tissue near the surface of the ovary and decidual cells have been described in the subperitoneal tissue of most of the lower abdominal organs. The writer has observed "glands" derived from an epithelial downgrowth which showed columnar epithelium and stroma containing decidual cells. The occurrence of this change can be of but little import in the determination of the endometrial origin of the perforating blood cysts.

These propositions will be elaborated further in a subsequent paper.

The *raison d'être* of the foregoing is to demonstrate that the implantation hypothesis, at least as far as the ovary is concerned, is not on a certain foundation. It is now proposed to show that a different point of attack gives other observations, which not only do not conflict with those of other observers but which may be used and coordinated into a useful and simple theory. It is necessary, at this stage, to review briefly the structure and physiology of the ovary.

MORPHOLOGY AND PHYSIOLOGY OF OVARY

The corpus luteum. The fundamentally important structure in the ovary is the ovum and this cell with its surrounding group of cells—the stratum granulosum—comprises the graafian follicle.

It is the cycle embodying the maturation and retrogression of succeeding generations of these structures which is responsible not only for the physiological changes in the genitalia but also for the many and varied bodies found in the ovary.

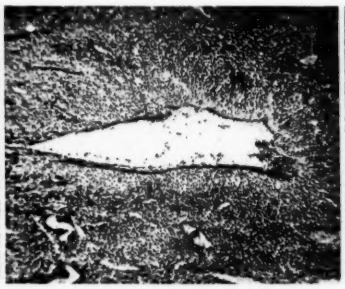
Maturation of the graafian follicle is associated with proliferation of the stratum granulosum and a change in the surrounding stroma cells to form the theca interna. The mature follicle consists of a thick stratum granulosum, in the center of which is the follicular cavity, a layer of swollen epithelium-like cells—the theca interna—and a circularly arranged layer of stroma cells, described as the theca externa. The ovum is contained in a mass of cells of the stratum granulosum which projects into the follicular cavity—the cumulus.

After migration of the follicle to the surface and rotation of the cumulus, rupture of the follicle with escape of the ovum occurs and is followed by a remarkable proliferation of the stratum granulosum, the cells of which give rise to the cells of the developing corpus luteum. Cells of the theca interna are in relatively small numbers and form an inconspicuous outer layer.

Hæmorrhage occurs into the luteal layer of cells and into the center of the corpus during the stage of vascularization.

Having reached the acme of its development, fatty changes occur in the cells and retrogressive alterations result in the gradual replacement of the luteal cells by hyaline tissue. The body thus formed is called the corpus albicans, and this has assumed its final appearance about 9 months after the formation of the corpus luteum. Elaboration of these changes is unnecessary in the presence

Fig. 1.



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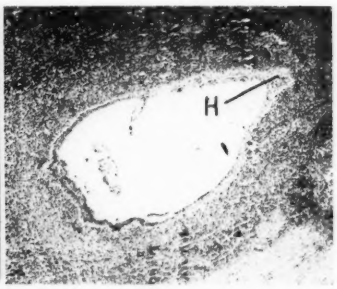

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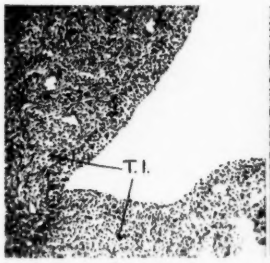

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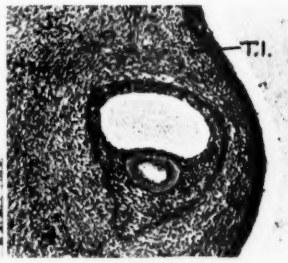

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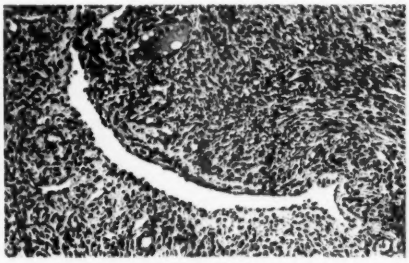
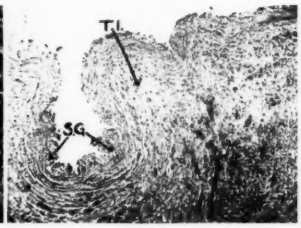


Fig. 6.

Fig. 7.



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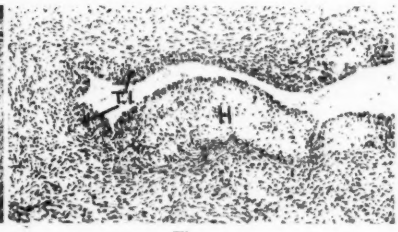


Fig. 9.

Fig. 1. A section of an ovary showing a retrogressing graafian follicle. The stratum granulosum is degenerating and the theca interna layer is proliferating. ×25.

Fig. 2. A stage in the progression of atresia of a graafian follicle, somewhat later than that shown in Figure 1. The stratum granulosum is disappearing, the theca interna is well developed, and in one part hyaline change is present. ×18.

Fig. 3. A cystic atretic follicle showing the disappearance of the stratum granulosum in one part with hyalinization of the theca interna layer, (*H*). ×13.

Fig. 4. Photomicrograph of a portion of the wall of a cystic atretic follicle. The stratum granulosum and the subjacent theca interna, *T. I.*, are present. ×60.

Fig. 5. Photomicrograph showing a retrogressing graafian follicle and also portion of the wall of a cystic atretic follicle. Theca interna, *T. I.* ×67.

Fig. 6. Photomicrograph of a small atretic follicle in which the stratum granulosum has disappeared. Hyaline change has commenced in the theca interna. ×85.

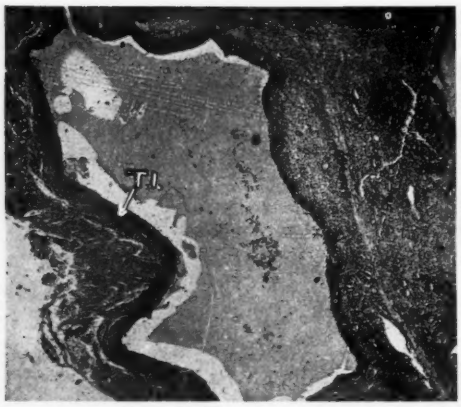
Fig. 7. Photomicrograph of a portion of the wall of another atretic follicle. Hyaline change is advanced further than it is in the specimen which is shown in Figure 6. ×120.

Fig. 8. Photomicrograph of a portion of the wall of a "granulosa luteal cyst." The tissue is partially hyalinized but remnants of both the stratum granulosum, *S. G.*, and theca interna, *T. I.*, may be seen. ×17.

Fig. 9. Photomicrograph showing a portion of the wall of a small collapsed atretic follicle. The theca interna, *T. I.*, is present and hæmorrhage, *H*, has occurred into it at one place. The stratum granulosum is present as a single layer of "epithelium." ×90.

of adequate descriptions in current textbooks and articles.

Corpus luteum cysts. A number of pathological conditions arise which correspond to the various stages in the life history of the luteal body. There are: (1) corpus luteum cysts, (2) corpus albicans cysts, (3) corpus luteum blood cysts, and (4) corpus luteum tarry cysts.



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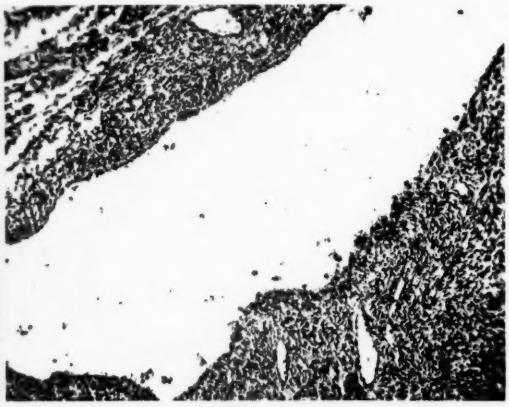

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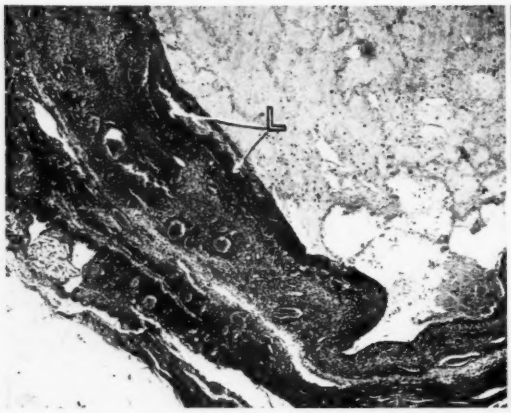

Fig. 12.

Fig. 13.

Fig. 10. Low power photomicrograph of a cystic atretic follicle. This atretic follicle was present in an ovary which contained many of the typical "perforating chocolate cysts." The theca interna is shown at *T. I.* ×13.

Fig. 11. Photomicrograph of a cystic atretic follicle which occurred among many typical "endometrial" cysts. ×75.

Fig. 12. Photomicrograph of a portion of the wall of a typical "endometrial" cyst. Although a portion of the wall was lined by epithelium in this part, there was typical luteal tissue, *L.* ×18.

Fig. 13. Low power view of a blood-containing cyst—macroscopically a typical endometrial cyst—occurring with many epithelium lined cysts. In the wall is an obvious layer of hyaline tissue. ×13.

1. Cysts of the corpus luteum are characterized by the presence of clear fluid in the cavity of an enlarged luteal body. It possesses typical luteal tissue in the wall and this shows the festooning which is observed in the normal corpus luteum.

The presence of a small amount of fluid is a constant finding in corpora lutea and this may be slightly increased in many cases, so that all gradations are found between the normal body with a little fluid in its central portion and a well formed cyst.

As the luteal body ages, the changes mentioned take place and these occur whether it has a very small cavity or is a comparatively large cyst. Thus cysts of the corpus luteum may show many appearances according to the amount of hyaline tissue and stroma tissue present in the wall. The end-result, when all the luteal tissue has disappeared and hyaline

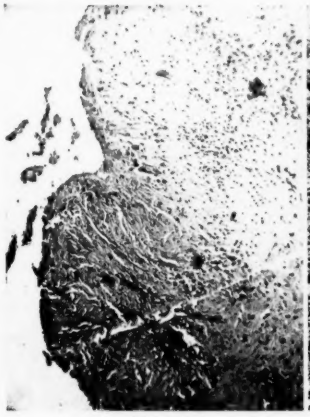

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Fig. 15.

Fig. 16.

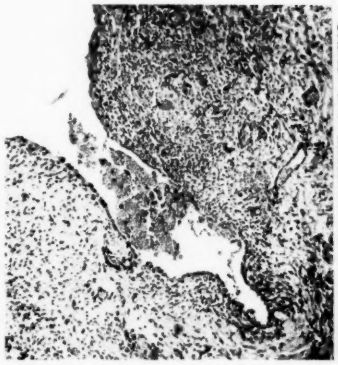


Fig. 17.

Fig. 18.

Fig. 19.

Fig. 14. A higher power view of portion of the wall of the cyst shown in Figure 13. ×38.

Fig. 15. Photomicrograph showing the typical appearance of a collapsed atretic follicle. The stratum granulosum is still present in part. Compare with the epithelium lined cyst shown in Figure 16. ×15.

Fig. 16. Photomicrograph showing an epithelium lined cyst—which, in portion of its wall was typically "endometrial"—arising from an atretic follicle. The gross similarity to an atretic follicle is shown by comparison with the cyst which is shown in the photomicrograph, Figure 15. ×15.

Fig. 17. Photomicrograph of a portion of the wall of an atretic follicle which is developing an epithelium lining. What relationship this new development bears to the cells of the retrogressing stratum granulosum is at present undetermined and is not of paramount importance from the point of view of the hypothesis given in this paper. ×25.

Fig. 18. Photomicrograph of portion of the wall of a blood cyst of the ovary. It is lined here by typical luteal cells, but in other portions of the cyst the lining is of the "endometrial" variety. ×38.

Fig. 19. Portion of the wall of a cystic follicle which is developing an epithelial lining. ×38.

tissue only is present, is the corpus albicans cyst.

2. The characteristics of the corpus albicans cyst will be apparent from the description given of its origin. The cyst contains in its wall, hyaline tissue which is developed from corpus luteum tissue. It is usually small and a typical example has an unmistakable appearance, though when but little hyaline tissue is present (in comparison with the amount of stroma tissue)—as happens in larger cysts—recognition may be more difficult.

Some writers doubt the occurrence of this cyst. Probably, the development of cystic changes in a corpus albicans does not take

Fig. 20.

Fig. 21.

Fig. 22.

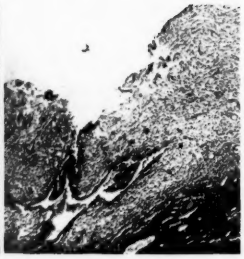


Fig. 23.

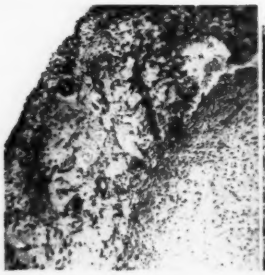


Fig. 24.

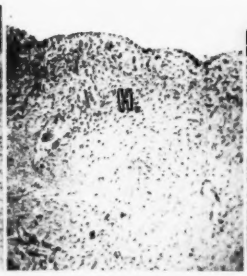


Fig. 25.

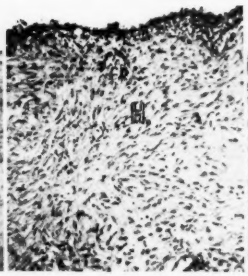


Fig. 26.

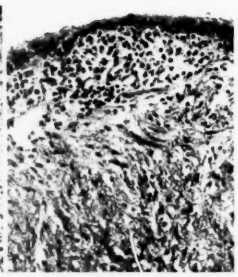


Fig. 27

Fig. 28.

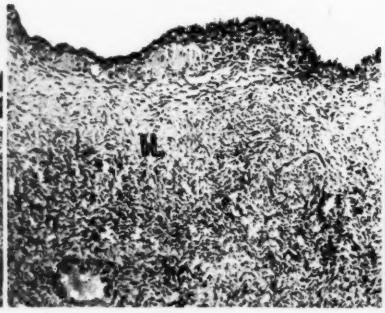


Fig. 29.

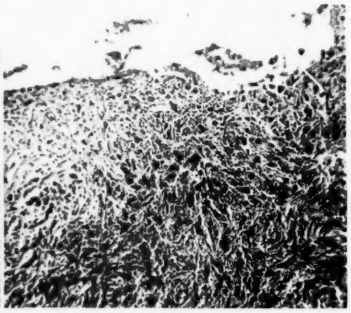


Fig. 30.

Fig. 20. Photomicrograph of a portion of the wall of an old luteal cyst—probably arising from an atretic follicle (see text)—showing the hyaline tissue in the wall and the epithelial lining. The hyaline tissue, *H*. ×10.

Fig. 21. Photomicrograph of a portion of the walls of a collapsed tarry or chocolate cyst of ovary showing one side lined by epithelium, *E*, the other hyaline tissue, *H*. ×15.

Fig. 22. Photomicrograph of a portion of the wall of an epithelium lined blood cyst of the ovary. The hyaline tissue which indicates origin of cyst is well seen. ×8.

Fig. 23. Higher power view of portion of the wall of the cyst shown in Figure 22. A typical "endometrial" gland is present; its relationship to surface cells is shown. ×20.

Fig. 24. Portion of wall of luteal cyst showing hyaline tissue, *H*, epithelium on surface, and subepithelial stroma, *S*. Hæmorrhage has occurred into stroma. ×40.

Fig. 25. Photomicrograph of a part of the wall of a blood cyst of the ovary showing the hyaline tissue, *H*, lying below the epithelium. ×60.

Fig. 26. Photomicrograph of portion of wall of cyst shown in Figure 24. The lining epithelium, a small amount of subepithelial stroma, and hyaline tissue, *H*, are shown. ×75.

Fig. 27. Photomicrograph of a part of the wall of another blood cyst of the ovary showing the epithelium, a subepithelial stroma more abundant than in the example shown in Figure 26, and underlying hyaline tissue. ×120.

Fig. 28. Photomicrograph of a portion of the wall of a blood cyst showing a well developed epithelium lining, an abundant stroma, and underlying hyaline tissue, *H*. ×60.

Fig. 29. Portion of the wall of a typical "endometrial" cyst of the ovary. Hyaline tissue, *H*, although relatively inconspicuous, may still be recognized. Other portions of the wall of this cyst contained more definite hyaline tissue and also luteal tissue so that the recognition of the nature of the cyst was not difficult. Such findings indicate the necessity for thorough investigation of these cysts. Some "pseudoxanthomatous" cells are present. ×67.

Fig. 30. Portion of the wall of a luteal tarry cyst. ×60.

Fig. 31.

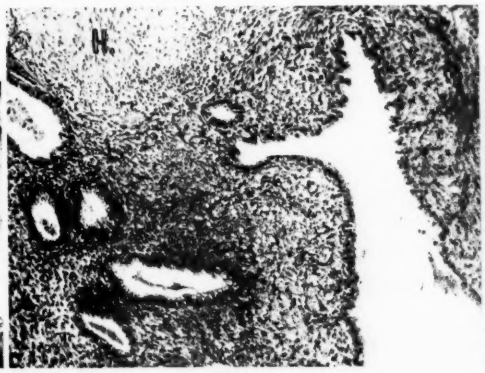


Fig. 32.

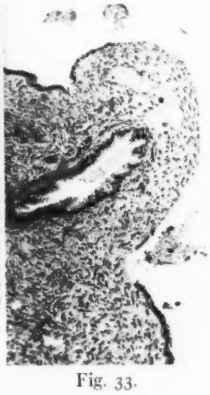
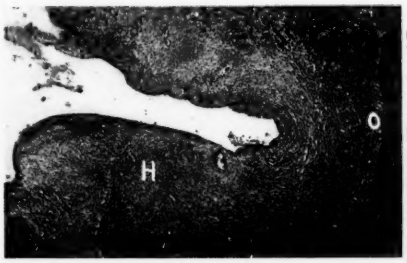


Fig. 33.



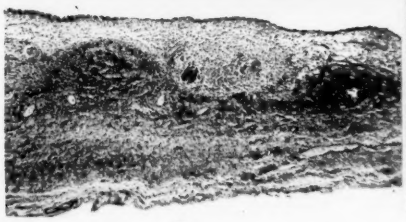


Fig. 35.

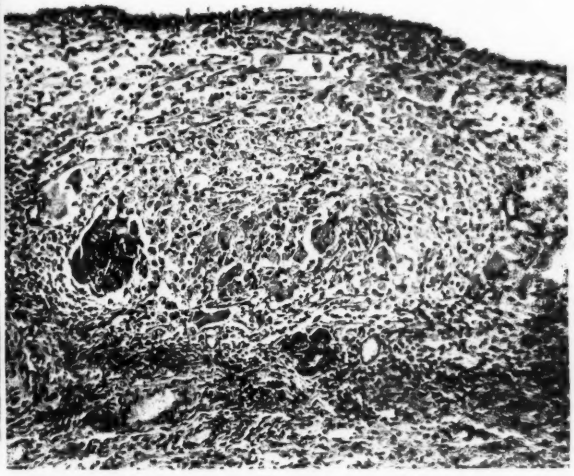


Fig. 36.

Fig. 31. Low power view of portion of a blood cyst of the ovary. It was lined by columnar epithelium with a subepithelial stroma (see Fig. 32). Its luteal origin is indicated by the presence of hyaline tissue (compare with Fig. 44) and the site of rupture of the graafian follicle which gave rise to the original luteal body may be seen at the depression on the surface of the ovary. ×10.

Fig. 32. Photomicrograph of portion of the blood cyst shown in Figure 31. The epithelium is columnar in type and crypts cut in section give the appearance of glands. Hyaline tissue which indicates the previous presence of the luteal tissue is shown at *H*. ×75.

Fig. 33. Photomicrograph showing a glandular space near the surface of the ovary. This was not an implantation but arose by continuity from the epithelium lining an old luteal cyst. This was demonstrated by serial sections. Compare with Figure 44. ×75.

Fig. 34. Photomicrograph of a portion of an epithelium lined tarry luteal cyst. The hyaline tissue is shown at *H*; ovarian tissue, *O*. ×12.

Fig. 35. A portion of the wall of a luteal cyst. ×20.

Fig. 36. Higher power view of portion of the wall of the cyst shown in Figure 35. The epithelium is columnar and a group of pseudoxanthomatous cells are present. ×98.

place, but that hyalinization occurs in the wall of a luteal cyst, no one who has examined these cysts can doubt.

It is of interest that the progress of the change in the wall of a corpus luteum cyst does not proceed uniformly in all parts and at the same rate; thus typical luteal tissue may be found in one portion and hyaline material in another part. Incomplete examination of such a cyst may lead, therefore, to the diagnosis of either luteal or corpus albicans cyst.

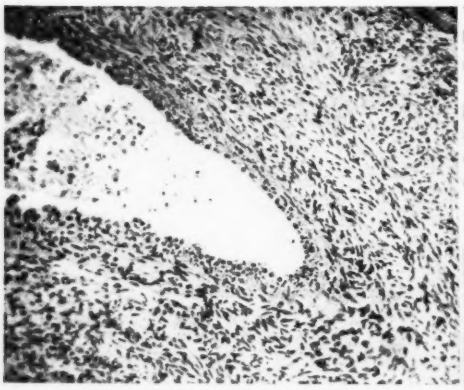


Fig. 37. Portion of an epithelium lined blood cyst of follicular origin. ×100.

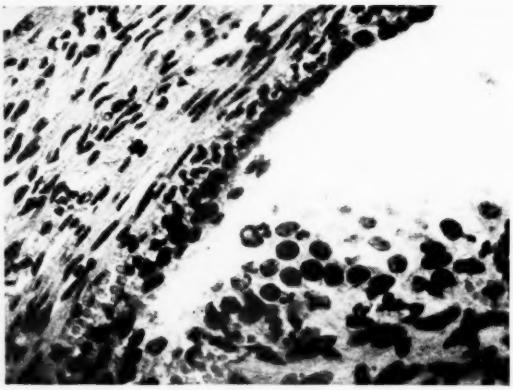


Fig. 38. Higher power view of the epithelium lining the cyst shown in Figure 37. ×375.

3. Luteal blood cysts. Since hæmorrhage occurs at the stage of vascularization of the corpus luteum and since cystic change may occur in this structure, the occurrence of corpus luteum blood cysts requires little discussion. In a manner similar to that described, all stages from the hæmorrhagic corpus luteum to the corpus luteum blood cysts several centimeters in diameter are revealed by an examination of these structures.

4. Corpus luteum tarry cysts. The change in the blood occurring in cysts of the ovary, from the normal to a tarry or chocolate consistency is a well recognized phenomenon. It is due to a physicochemical change, which is merely an indication of the age of the blood. Similar changes are observed in blood in other parts of the body.

The tarry corpus luteum cyst shows the festooning of the wall which characterizes the original body. This is important in the differentiation of the cyst from some to be mentioned subsequently.

All of these cysts are important owing to the occurrence of certain secondary changes.

In a classification proposed by Fraenkel in 1898, luteal cysts of three types were described: (1) those lined by luteal cells, (2) those lined by fibrous tissue, and (3) those in which a heterotopic epithelium lined the cyst on the inner aspect of the connective tissue (Fig. 48).

It is the third group in which we are interested. Any of the various cysts which have been mentioned previously may show this heterotopic epithelial lining.

It consists of cells of columnar, cuboidal or flattened form, with a subjacent "stroma" of round and spindle cells which often support a number of phagocytic cells. Beneath this "stroma" is the tissue proper of the luteal body—either luteal cells or hyaline tissue.

Crypts may be present in the wall of the cysts and the epithelium lining these may, owing to the peculiarities of the direction in which the section has been made, show "gland-" like structures. The epithelium often lines only a portion of the cyst wall.

This epithelium is the keystone on which the conclusions produced in this paper depend.

The atretic follicles. The ovary, at birth, contains about 70,000 ova, and during the normal sexual life of the individual only 500 (approximately) of these come to maturity and since the follicles which mature and form corpora lutea are relatively few, it is very important and highly instructive to inquire into the fate of the remainder.

At the commencement of the intermenstrual cycle, a number of graafian follicles approach maturity. Rupture of one follicle is followed immediately by the retrogression of the others and it has been shown experimentally that this is due to a hormone derived from the developing corpus luteum.

This retrogression of the follicles (atresia) is characterized by the disintegration of the

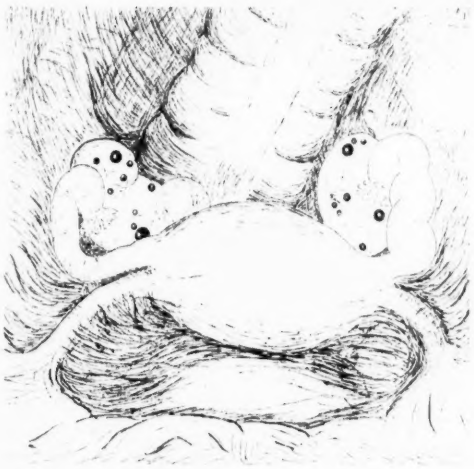


Fig. 39. Drawing showing the appearance presented by a typical example of the blood cysts as seen at operation.

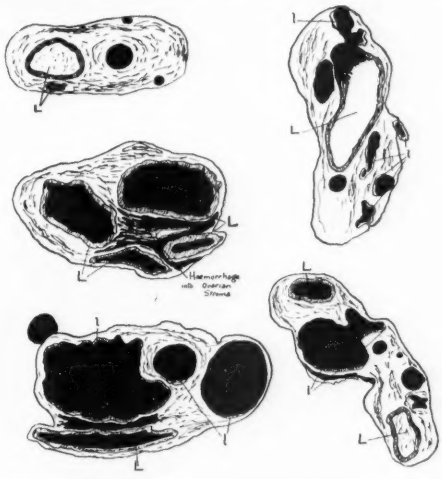


Fig. 40. Drawing of the appearances presented on section of right ovary removed in case shown in Figure 39.

stratum granulosum and a proliferation of the theca interna cells. The typical atretic follicle shows an appearance which is the reverse of that seen in the corpus luteum: i.e., a well marked theca interna layer and a very poorly marked or almost absent stratum granulosum.

The theca interna cells proliferate and swell until they resemble luteal cells. They may accumulate pigment and they are arranged in a radial fashion around the cavity of the follicle.

Changes comparable with those seen in the corpus luteum now occur. Fatty changes take place in the cells and they become replaced by hyaline tissue. Various hyaline bodies result—the corpus atreticum, the corpus candicans, and the corpus fibrosum.

It will be seen that since these various structures are many times more numerous than the luteal bodies and their derivatives, the follicles, their derivatives and the pathological conditions arising therefrom are highly important in the elucidation of multiple cysts of the ovary.

Cysts arising from the atretic follicle. Dilatation of atretic follicles occurs in any of the stages of their development and several cystic structures may result. In addition, hæmorrhage gives certain modifications. Many varieties may be considered, under the following headings: (1) follicular cysts, (2) follicular blood cysts, (3) follicular tarry cysts (tarry "luteal" cysts).

The follicular cysts are among the commonest structures met with in the ovary. The vast majority are small and are merely minor variants of the normal process of retrogression of the graafian follicle. On the other hand, large cysts may develop from the atretic follicle. The largest cyst which the writer was able to demonstrate as being of this origin was 14 centimeters in diameter. All of these

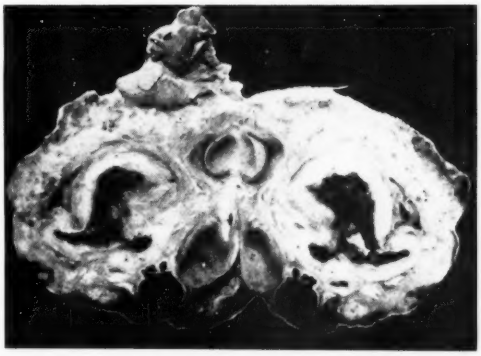


Fig. 41. Photograph of an ovary showing a luteal cyst, a follicular cyst, and an endometrial cyst. This last was developed from an atretic follicle.

Fig. 42.

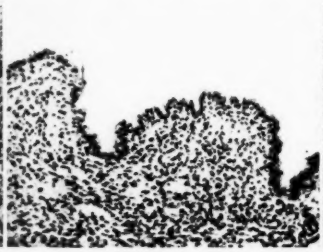


Fig. 43.

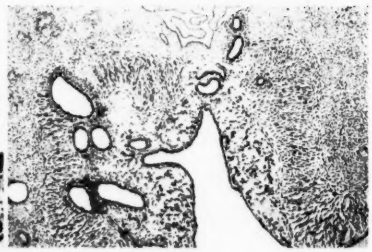


Fig. 44.

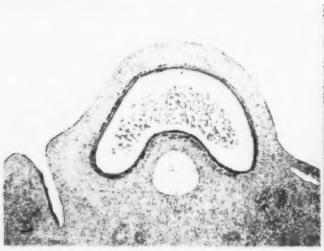


Fig. 45.

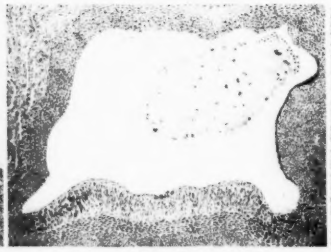


Fig. 46.

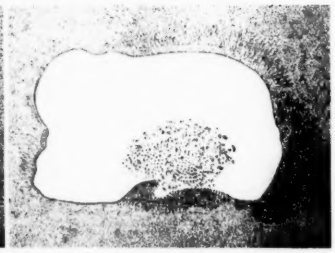


Fig. 47.

Fig. 42. Photomicrograph of a typical gland which might be described as "endometrial." Considered apart from its relationships, there is no indication of its nature or origin. ×110.

Fig. 43. Photomicrograph of a portion of an "endometrial" cyst similar to that seen in Figure 42. Investigation of other portions of its wall indicated its follicular origin. ×110.

Fig. 44. A composite drawing based on sections made of the cyst shown in Figure 31. The hyaline tissue is slightly exaggerated in order to render the relationships of the tissues more clear.

Fig. 45. Drawing of a follicular cyst lying near the surface of the ovary. It is lined by epithelium and the hyaline tissue indicates that it is of follicular origin and is not due to implantation.

Fig. 46. A drawing made from serial sections showing a blood cyst which is lined partly by luteal tissue, partly by hyaline tissue, and in part by columnar epithelium with no subjacent tissue of luteal origin.

Fig. 47. Drawing of a cyst showing luteal tissue in portion of the wall, hyaline tissue in a considerable portion and the remainder showing only columnar epithelium. It will be seen that if the section were taken in another direction only hyaline tissue would be present to give the clue of the nature of the cyst and in some cases even this may be absent.

cysts show a definite theca interna layer of cells with a few cells of the stratum granulosum on the inner aspect.

As the cyst ages, hyaline changes occur, comparable with those seen in the small retrogressing follicle. Thus not only are there corpus candicans cysts, but all intermediate stages are to be found. The corpus fibrosum is a variation from the normal hyaline body, in which fibrous tissue is formed instead of hyaline material. In some of these cysts there may be fibrous tissue in the whole or in portion of the cyst wall. Usually, however, it is possible to find hyaline tissue in some or other portion of the wall, so that there need be no doubt as to the origin and nature of the structure. Sometimes old hyaline bodies are found in the ovary and it is not possible to determine their origin, and similarly some cysts may defy classification. This applies particularly to the differentiation of cysts of atretic follicle and corpus luteum origin, in their later stages.

"Luteal" cysts of follicular origin. The usual sequence of events during atresia is a retrogression of the stratum granulosum and a proliferation of the theca interna cells and a "luteal" change in these cells. In one well known condition, however, although the follicles are undergoing atresia, the stratum granulosum proliferates as well as the theca interna. This is the multiple luteal cyst associated with hydatidiform mole. A great deal of discussion has waged around the origin of these "luteal" cells. The follicles do not rupture on the surface, and the ovum

dies, so that the cysts belong to the retrogressive or atretic series, and it was thought that the cells arose, as usual, from the theca interna layer. It has been demonstrated by Strassmann, however, that they arise from the cells of the stratum granulosum.

There are, therefore, two varieties of follicular cysts:

(1) In which there are a well developed theca interna layer and an extremely poorly marked stratum granulosum layer; (2) in which representatives of both layers are well marked.

Blood cysts. Hæmorrhage occurring in the corpus luteum and its derivatives occupies the stratum granulosum and from this ruptures into the central cavity. In the case of the typical atretic follicle, hæmorrhage takes place in the theca interna cell layer and may rupture into the surrounding tissue. Pressure inward pushes the stratum granulosum before it so that blood does not usually occupy the cavity of the follicle.

Statements are sometimes made that hæmorrhage never occurs into the follicular cavity, but this is not correct. The writer has frequently observed blood in follicular cysts in hyperæmic conditions of the ovary and in the ovaries which contain multiple blood cysts.

As with the corpus luteum blood cysts, the cyst wall may show any of the stages of retrogression from the typical luteal cells (theca interna in origin) to typical hyaline or stromal tissue with a complete absence of luteal cells.

Tarry cysts of follicular origin. These cysts have been considered in several papers which are referred to in a paper recently submitted by the writer (3). Changes in the blood occurring in the cysts just described are responsible for the character of the fluid in these cysts.

Since there are two main varieties of follicular cysts, so two principal forms of tarry luteal cysts of follicular origin may be differentiated: (a) the tarry theca luteal cyst, (b) the tarry granulosa luteal cyst.

These names were suggested by Shaw to indicate that in one cyst the cells were probably of theca interna origin while in the other, cells of the stratum granulosum are also present.

It was pointed out in the paper mentioned that the cells occurring in the walls of these cysts are of atypical luteal character and since they become replaced gradually by a connective tissue, all stages may be found between the easily recognizable cyst containing well marked (if atypical) luteal cells and the one in which few luteal cells are to be found.

Secondary changes. The importance of the development of a lining of heterotopic epithelium in the case of the corpus luteum cysts has been mentioned. This lining is to be found both in corpus luteum cysts and in the cysts of follicular origin. The epithelium has the same characteristics as in the corpus luteum cysts—may be columnar, cuboidal, or flattened in shape and there is present a subepithelial "stroma."

The cysts possessing this lining are of extreme importance in this discussion, so that they will all be considered, at this stage, in further detail.

EPITHELIUM-LINED BLOOD CYSTS OF THE OVARY

A cursory survey of the foregoing descriptions shows that there are a large number of cysts of the ovary which possess columnar or cuboidal epithelium lining. These cysts do not present, in reality, as formidable an array as might be expected, since they are but modifications of the normal elements found in the ovary and do but correspond to these various structures, and can be simply classified.

If any one of these cysts be considered apart from its fellows, it immediately becomes difficult of analysis and comprehension. It seems to me that many of the difficulties that have arisen in the interpretation of the blood cysts of the ovary, are due to such segregation of material from its physiological and morphological context. Hence, it is necessary, when examining epithelium-lined structures in the ovary to determine to which of the bodies of the series already described they are related.

From the description previously given, it may be deduced that numerous atypical forms are to be met: e.g., owing to the irregular rate of progression of the various processes taking place in the wall, but in the vast majority

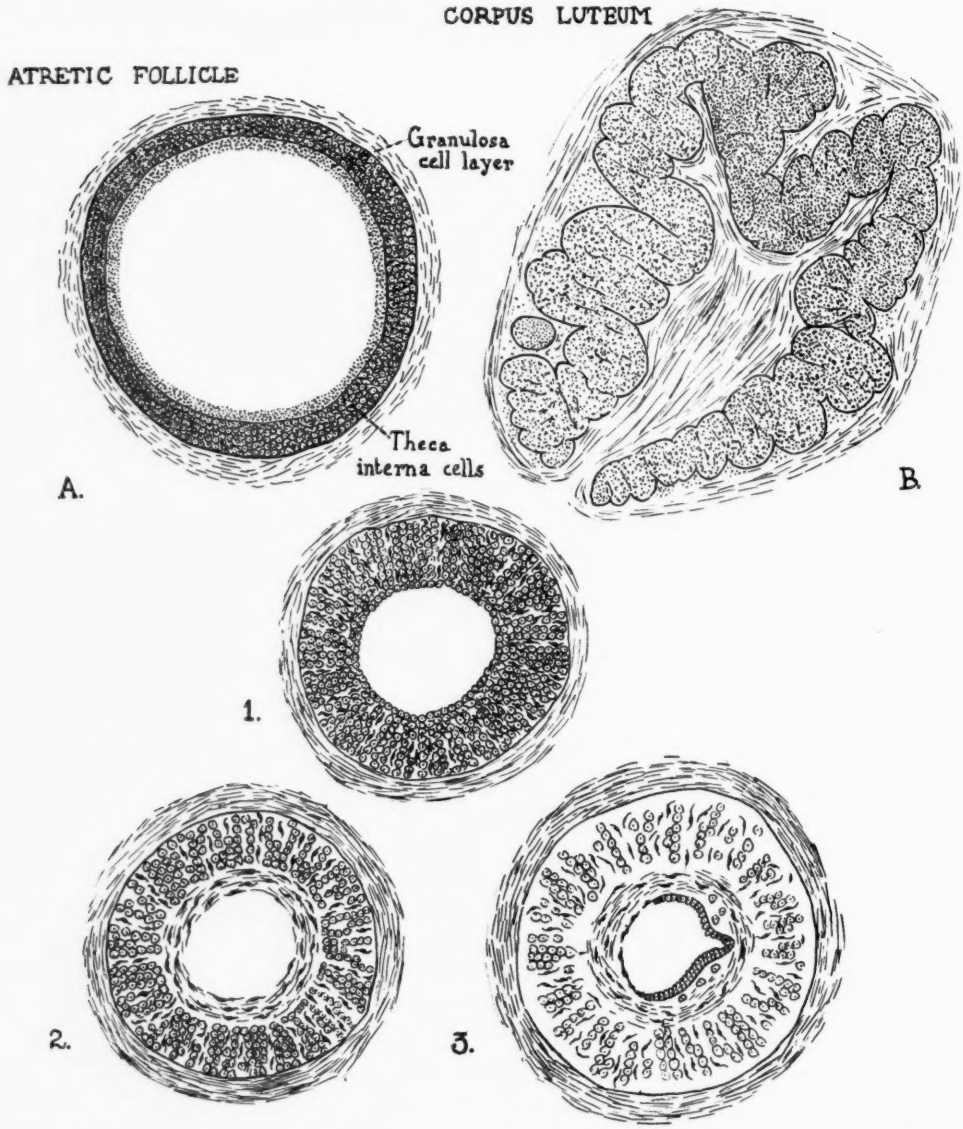


Fig. 48. Diagrammatic representation of the relationship of the various luteal cysts and the atretic follicles and luteal bodies. Both these structures give rise to cysts which contain luteal cells in their walls. The cyst may be lined: (1) by the luteal cells; (2) by connective tissue lying internal to the cells; (3) by a heterotopic epithelium which develops on the internal aspect of the connective tissue.

of cases some part or other of the wall gives a clue to the nature of the cyst.

In summary, the various cysts observed are:

A. Corpus luteum cysts; corpus albicans cysts; follicular cysts which may also become hyaline.

B. Blood cysts of various types.

C. Tarry cysts: (a) corpus luteum cysts, (b) tarry theca luteal cysts, and (c) tarry granulosa luteal cysts.

Many variants of these forms may arise. Any of these cysts may possess an epithelial lining.

A description of some of those which have been investigated by the writer may be of interest.

For the reasons given previously, cysts of the corpus luteum series are comparatively uncommon. One of these is shown in Figures 31 and 44. Strong evidence for the conclusions concerning its origin can be obtained from the examination of even a single section. Thus the depression on the surface of the ovary where the cyst comes closest to this surface is very apparently the site of rupture of the originating graafian follicle. The hyaline tissue is well seen round the wall of the cyst. The differences between typical compact hyaline tissue of a corpus albicans and the semifibrous hyaline tissue observed in the wall of such cysts as this seems to be explicable readily by the difference in the conditions of their formation, position, and relationships. The other cysts which were present in this ovary were all of the atretic follicular type.

Some of the cysts of the atretic follicular series are almost perfect specimens. Such a one is shown in Figure 45. This cyst, when seen macroscopically, seemed to be an excellent example of implantation, but microscopic examination showed that it was a hyalinized atretic follicle which had developed an epithelial lining.

The majority of the cysts, as previously stated, do not give such a typical appearance. Different stages of retrogression of the luteal cells may be observed in various portions of the cyst wall. Thus, in one area luteal cells (atypical but recognizable) will be found; in other parts hyaline tissue; and in still others no definite evidence whatever of the nature of the cyst is obtainable. Such a cyst is shown diagrammatically in Figure 47. This cyst was so demonstrated by a lucky section and it was such appearances that first suggested to the writer the mode of formation of such cysts as those under consideration. It was later that the importance of the hyaline tissue—in the absence of luteal cells—was appreciated.

It will be seen that in such a cyst the epithelium does not extend throughout the whole extent of the wall, and it is usual for the epithelium to be present only in those parts in which luteal cells are absent. This is of very considerable importance. Should the section happen to be taken in a plane at an angle, e.g., right angle, to that shown in the figure, it will be apparent that one section, taken at one end of the cyst may show only the epithelium in the wall, and the one taken at the other end of the cyst may show only luteal tissue in the wall. Without serial sections, it would be concluded, almost certainly, that different cysts were being investigated.

That the importance of hyalinized tissue in the wall of these cysts has not been appreciated is apparent from a perusal of many of the reports of "endometrial" glands and from an examination of accompanying illustrations. Hyaline tissue has been remarked upon as an apparently casual observation by many writers.

It might be mentioned here that phagocytic cells (pseudoxanthomatous) are often present in large numbers in the walls of these cysts, and it is important that they should be distinguished from luteal cells. Their morphology, arrangement, and relationships to the surrounding tissue render this a matter of relative simplicity.

In some of the cysts, though portion of the wall shows evidence of luteal or hyaline tissue, other parts are formed by ovarian stroma directly underlying epithelium without any suggestion that hyaline tissue had ever been present originally (see Fig. 46). No adequate explanation is available, though it is possible that the distention of a cyst was too great or too rapid to allow commensurate stretching of the luteal or hyaline portion of the cyst wall so that the cyst contents, in some portions, have come into contact with the ovarian stroma and subsequently the epithelium has grown over this. However this may be, the presence of ovarian tissue in the immediately subepithelial portion of the cyst wall is of common occurrence. No example of

this association of the ovarian tissue with the epithelium throughout the whole wall has yet been observed by the writer. In all cases there was some evidence of the presence of the luteal or follicular material. It is not intended that this statement should suggest that this may not occur, but that its occurrence is uncommon and in any apparent example, serial sections are essential to determine the accuracy of the observation.

The epithelium. The epithelial cells which line these cysts have been described. Their shape varies in different places. There is usually a single layer. Where the cells are columnar the nuclei are basal in position. The cells, in some cases, resemble the cells of the endometrial lining but more frequently they do not, especially when they become cuboidal or flattened. The columnar cells may rest on an apparent basement membrane though some seem to be semisyncytial in form and to be continuous with the subjacent tissue cells.

Although the morphological characters of the tissue of the so-called "endometrial" glands are said to be almost identical with those of endometrium, a reference to descriptions and illustrations shows that a great deal of latitude is allowed in interpretation. Thus the cells are just as reminiscent of epithelial cells in other parts of the body and in many cases they do not, in any way, simulate endometrial epithelium.

The stroma. Beneath the epithelium in these cysts, there is usually a collection of round or spindle cells packed more or less closely together, and this tissue may closely resemble the subepithelial stroma of the uterus.

In many cases, however, the resemblance is very remote. This does not affect the conclusions which are here given, since the license used in the descriptions of the epithelium of the "endometrial" glands is also exercised in the case of the stroma which is described as being at times scanty or absent.

Where the epithelium lines a surface without irregularities, the subepithelial stroma is scanty, but it is abundant around crypts and "glands."

Epithelium-lined glands. Crypts in the walls of these tarry cysts are common and these are lined, almost invariably, by columnar epithelium, even when the surfaces of the main cavity are lined by flattened cells or where even these are absent.

These projections of the central cavity may extend for a considerable distance and owing to a meandering course, the plane of section may cut these crypts in one or more places. The appearance of "glands" thus obtained is not uncommon in the walls of these cysts.

As stated, the subepithelial stroma is particularly abundant around these glands, so that it is these more particularly which give a close imitation of endometrium.

An important feature, which is illustrated in Figure 44 is the projection of these crypts beyond the boundaries of the original cyst wall, i.e., beyond the area containing hyaline tissue. Thus it is possible to discover "glands" in ovarian tissue without any proximate evidence of derivatives of luteal or follicular bodies. Figure 33 shows such a gland space which was shown by serial section to be in continuity with the central cavity of a luteal cyst. In the absence of this evidence, such a gland would be regarded as of "endometrial," that is implantation, origin.

The invasive properties of this epithelium here illustrated, are extremely important from the point of view of the results of rupture of these cysts with spilling of their contents into the peritoneum. This is discussed later.

The origin of the epithelium. No unanimity of opinion has been reached concerning the origin of this epithelium. Three hypotheses have been advanced:

1. An origin from the surface epithelium of the ovary.

2. An origin from the endothelium of vessels lying in the connective tissue lining the wall of the cyst.

3. An origin from luteal cells or their progenitors.

That the epithelium lining the walls of some of the luteal cysts is continuous with and presumably developed from the surface epithelium is easily demonstrated in some examples. The ease with which the surface epithelium grows into any space in the ovary communicating with the surface renders such an explanation reasonable for these cases.

The majority of cysts cannot come into this category, however, since most of the graafian follicles do not rupture and consequently their cavities do not become continuous with the exterior.

Appearances occasionally suggest that the endothelium of the vessels in the connective tissue may proliferate, form a lining to the cyst, and become columnar. Though endothelium is known to change shape in this fashion, the evidence in the case of these cysts is not in any way conclusive. This suggestion is similar in kind to that made by Schiller in which aberrant endometrium arises by metaplasia of lymphatic endothelium.

Fraenkel suggested originally that the cells arise from luteal cells. Although the evidence is inadequate, as yet, observations made by the writer point in this direction. Certain well known phenomena suggest this origin also: (1) A columnar epithelium may be found in simple atretic follicles. Continuity between these cells and cells of the degenerating stratum granulosum may be observed. (2) The life history of the epithelium (the formation of glands, the effects of rupture of the cysts, and the development of tumors) more strongly suggests an epithelial (luteal) than an endothelial origin.

The origin of this epithelium is not of paramount importance in the considerations arising in this paper, except that it arises probably by metaplasia from cells which are present in the ovary, and not from cells of another organ by a peculiar process of transplantation.

Endometriosis. Let us pause to consider the condition of multiple blood cysts of the ovary from the point of view of the protagonists of the transplantation hypothesis.

The condition found in the ovary consists of numerous blood cysts, and blood is found both in the cavities and in their walls. They are lined by an epithelium which, in a typical case, is columnar but may be cuboidal or flattened (stated to be by the pressure of the cyst contents). Beneath the epithelium, there is a stroma of spheroidal cells which resemble the immediately subepithelial tissue in the wall of the uterus. In some circumstances this may be scanty or absent.

Most reports and descriptions recognize some follicles or luteal bodies in the organ, but these are regarded as incidental. The presence of hyaline tissue in the wall of some of the cysts has been mentioned.

The difficulties in the acceptance of the implantation hypothesis are several: (1) The absence of epithelium (or the extreme flattening of epithelium) and the absence of "stroma" which may occur over large areas of the cyst walls renders necessary the further hypothesis—of destruction or distortion of these tissues. Their original presence on those areas in which it is not found is pure assumption. (2) The hypothesis ignores the hyaline tissue which is present in the walls of some of the cysts. (3) It overlooks the associated small cysts of the ovary which are of follicular or luteal origin and therefore overlooks completely, the normal processes of the organ involved. (4) It takes no cognizance of the pathological changes in tarry luteal cysts.

Suppose we turn now to the physiological changes, which play an important part in the implantation hypothesis. Hæmorrhage occurs in these cysts in association with the menstrual period. It is known, however, that hæmorrhage into luteal cysts occurs at these periods also. I have observed, at operation, bleeding from a tarry luteal cyst (proved by subsequent section) during a menstrual period—both tarry material and fresh blood were present. The occurrence of hæmorrhage, therefore, does not necessarily support an endometrial origin.

The *complications* which are most important are (1) rupture of the cysts with the formation of secondary growths on the peritoneum and (2) the development of carcinoma in "endometrial" cysts.

Rupture of these ovarian cysts with the formation of secondary cysts in the peritoneum is accepted by Sampson. He considers that the ovary provides a "suitable soil" for the early growth of the cysts. Why is it, though, that "endometrial" growths do not occur in the peritoneum more frequently without the involvement of the ovary? In this respect, it should be noted that sometimes microscopic examination of ovaries which appear to be normal and which are

associated with peritoneal cysts show also the epithelium lined cysts.

If we grant that the ovary is the starting place for abdominal blood cysts, then both the implantation hypothesis and the tarry cyst suggestion are on common ground, because the transperitoneal spread of tissue in the peritoneal cavity, after the rupture of a cyst, is a well recognized phenomenon.

The ability of the glands arising in the tarry cysts to invade tissue is shown by their development beyond the confines of the wall of the original cyst (Figs. 32 and 44). That they should develop further when spilt into the peritoneum is therefore not surprising.

As to the development of carcinoma, Sampson has postulated, for some of the carcinomata of the ovary, an origin from the epithelium lining the "endometrial" cysts. These tumors may arise just as readily from the epithelium lining tarry cysts. Shaw and the writer have described such cases (2).

The resemblance between typical "endometriosis" and the epithelium-lined tarry cysts was discussed previously by the writer (3). At this time there were one or two examples concerning which the evidence for the follicular origin was inadequate, and an open mind was kept concerning them. Still the inference that both conditions were in reality the same seemed very strong. Subsequently the evidence in these cases has been forthcoming.

This study was commenced and indeed carried to its present conclusion from considerations of the ovarian cysts. Observations of other apparently related cysts have been made, however, and from the point of view of this study appear to fall into five groups: (1) ovarian cysts, (2) peritoneal cysts, (3) incisional cysts, (4) uterine cysts (adenomyomata), and (5) certain miscellaneous cysts, e.g., umbilical.

Ovarian cysts are here discussed and whichever hypothesis is adopted, such cysts appear to be the origin of many other cysts.

The peritoneal cysts are produced, in almost every case, by the implantation of epithelium in the peritoneum (a different proposition from the regurgitation of pieces of tissue of dubious viability through the fallopian tubes) from tarry cysts. Even the vaginal cysts may be explained by the burrowing of the "glands" through the vaginal vault from the pouch of Douglas, which is an early site for the implantations after the rupture of cysts. The burrowing propensities of the glands in the tarry cysts has been noted. These peritoneal cysts depend on the cysts of the ovary and do not present any serious difficulty to the acceptance of the hypothesis of the luteal origin of the tarry cysts. It should be noted however that the serosal hypothesis must be seriously considered and may prove to be the explanation of some of the peritoneal examples (see endometrial cysts of umbilicus).

The cysts occurring in incisions require little mention, since they may be called to assist any hypothesis. Other covering tissues, e.g., skin, may produce cysts after their implantation. This result might be expected from some of the experimental work on implantation of tissue.

The adenomyomata of the uterus and rectovaginal septum, for the present, fall into a separate category.

The endometrial cysts of the umbilicus present a difficult problem, whichever view of causation is favored. The writer is disposed at present to accept the serosal suggestion of the development of these structures. It is possible to correlate this with the tarry luteal cyst idea, but any complication of the discussion is to be deprecated at this stage.

SYMPTOMATOLOGY

Only one symptom requires special mention and that is sterility. It is the most constant symptom and often it is the one which brings the patient for treatment.

The explanation given usually is that some mechanical factor such as the adhesions which are almost invariably present or some intrauterine obstruction, which may have caused the reverse flow of menstrual fluid through the tubes, e.g., a fibromyoma or other factor, prevents the passage of the ovum into the uterus. It is well known, however, that extraordinary obstructions may be surmounted by the ovum in other conditions, so that some further explanation seems necessary.

The examination of the ovaries which are the site of multiple tarry blood cysts shows a number of atretic follicles and their derivatives and an occasional corpus luteum derivative, but actual corpora lutea are rare. Those which are present are atypical and aged. Here then, is an explanation of this interesting symptom: the graafian follicles have not ruptured onto the surface of the ovary with the subsequent formation of a corpus luteum, but have, instead, undergone retrogression. This introduces the problem of etiology.

ETIOLOGY

The causation of the luteal cysts and especially the tarry cysts is shrouded in mystery.

A number of observations are available, but a physiological correlation is not possible at present.

The retrogression of the maturing graafian follicles which follows the rupture of one follicle and the formation of a corpus luteum suggests the action of a hormone.

The demonstration, by Aschheim, that hormone from the pituitary gland plays a part in the causation of the multiple luteal cysts associated with hydatidiform mole shows that not only the genitalia but other ductless glands must be considered.

As stated, here is but a ray of light. It remains for future research to dispel the obscurity of this subject.

SUMMARY

1. Where speculative variations of several pathological principles are required to "explain" a pathological phenomenon, the explanation advanced is probably wrong and suggests the necessity of reviewing the observations on which it is based. It will be found that well established pathological principles suffice when the observations are sufficiently complete and carefully analyzed.

2. The implantation suggestion concerning "endometriosis" of the ovary requires for its foundation, hypothetical phenomena which have but doubtful counterparts in other portions of the body.

3. Pathological principles governing the interpretation of phenomena are distorted thereby.

4. An application of these principles to the multiple blood cysts leads to different conclusions, further observations, and an alternative hypothesis.

5. A résumé of the life history of the ovarian structures is given and an explanation of the blood cysts in terms of these structures is proposed.

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MUSCULAR RELAXATION PRODUCED BY NOVOCAIN AS AN AID IN TENDON REPAIR[1]

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THE present study was stimulated by the difficulties encountered in attempts at tendon suture. Our clinical experience led us to believe that retraction of the proximal end of the cut tendon was one of the most formidable obstacles to immediate suture and subsequent repair. We likewise felt that the development of a method which would either diminish or abolish this retraction would serve to decrease the number of failures in tendon suture. It seemed evident that relief of tension on the suture line would favor union, permit of the use of less suture material, and lessen the likelihood of the tearing out of the sutures used in repair.

Recently, Moser suggested a method of overcoming the retraction of the muscle tendon. He produced muscular relaxation by the intramuscular injection of tutocain through a transverse incision over the belly of the muscle involved. He termed this method transverse incision anæsthesia and regarded it as an important part of tendon suture. No mention was made of the extent and duration of the relaxation of the muscle nor was there offered any explanation of the mechanism by which this relaxation was produced.

It was our impression that the suggestion of Moser should be studied in greater detail with a view of more clearly establishing its clinical value.

The extent to which tendons do retract was brought out by Bonikowsky. He made observations on patients who sustained severances of the flexor tendons of the forearm and was impressed with the relationship existing between the extent of retraction and the total length of the muscle tendon proper. He found, when a tendon was severed, that the proximal end retracted and that the distance between the two cut ends represented, in most instances, one-seventh of the total length of the muscle tendon as measured from the point of origin to its insertion. He made use of these observations in subsequent cases by making a transverse incision over the calculated site of the end of the retracted tendon. Through this incision he could thread the proximal end through its sheath to the site of the original wound and thus effect tendon suture. This technique eliminated the danger of contaminating the tendon sheath by manipulations from below designed to locate the retracted tendon.

In 1882, Madelung described a similar procedure except that the distance of the transverse incision from the site of injury was left to the judgment of the surgeon and the stump was not always found at the selected level.

Certain phenomena have already been definitely established as occurring in muscles subsequent to the severance of their tendons. There also exists a rather comprehensive knowledge of the effects of the injection of local anæsthetics into skeletal muscle.

When a tendon is severed anywhere along its course, the proximal end retracts, leaving a gap between the cut surfaces. The separation of the cut ends is due to a contracture of the muscle. The initial phase of contracture is termed primary hypertonic contracture. It is brought about by a continuous stream of nerve impulses reaching the muscle from the central nervous system. If approximation of these cut surfaces of a tendon is not made at once, the gap between them increases until it reaches a fixed distance, the muscle passing into a secondary state of contracture to which the name myostatic contracture is given. Myostatic contracture is defined by Ranson as the fixation or setting of an immobilized muscle in a new and shorter than normal resting length. This condition does not take place in the whole muscle at once but develops gradually probably by different muscle fibrils becoming involved consecutively. It is the summation of these individual changes which finally determines the extent of the shortening. The terminal state of muscle change passing through primary hypertonic

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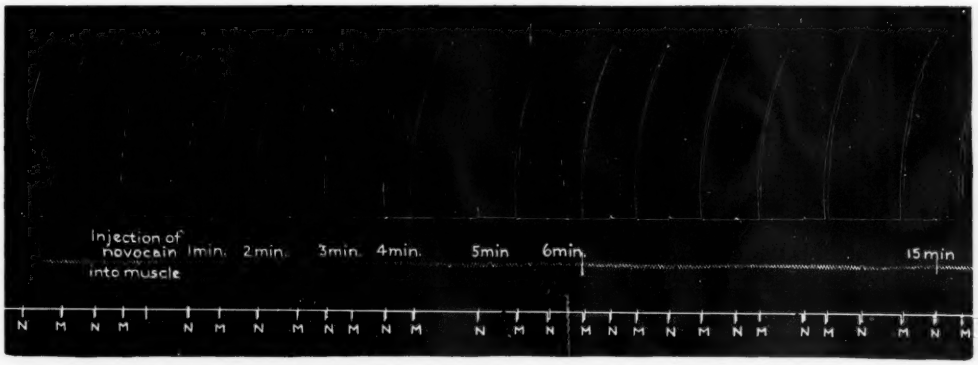

Fig. 1. Alternate stimulation of muscle and nerve showing gradually decreasing response of muscle to nerve stimulation following injection of ½ cubic centimeter novocain (1 per cent) into muscle belly. Direct stimulation of muscle unaltered.

contracture then secondary myostatic contracture is muscle atrophy. Functionally, a muscle in myostatic contracture cannot shorten as much as a normal muscle although the rate of relaxation is unaffected. The extensibility of the muscle is likewise decreased but this decrease is due to a loss of ductility, the elasticity remaining normal.

In the preceding discussion, we have assumed that the nerve muscle mechanism is intact. If the nerve supply to the muscle tendon is removed at the time of tenotomy the normal sequence of primary hypertonic contracture and secondary myostatic contracture with eventual atrophy does not follow. Ranson and Dixon found that 15 days after section of the tendo achillis, the gastrocnemius of the white rat had not only undergone shortening but it had also become set at a new length and was less extensible than normal (myostatic contracture). That it was due to a change in the muscle was made apparent when it was demonstrated that it persisted after section of the sciatic nerve. They further showed that if the sciatic nerve were cut at the time the tendon was severed, the changes in the muscle did not occur. This makes clear the dependence of the development of the myostatic contracture on the existence of the initial hypertonic contracture. It has also been shown by Froelich and Meyer that immobilization of a denervated muscle does not cause it to alter its extensibility or to become fixed. From the foregoing, it may be concluded that the development of myostatic contracture is dependent upon an uninterrupted nerve muscle mechanism.

In view of the nature of the secondary or myostatic contracture, it is apparent that once this condition has developed, tendon suture would be difficult to accomplish without undue tension. It is also clear from the above that any method which would remove the influence of the nervous system from the muscle following tenotomy would prevent this secondary contracture and thereby make it possible to approximate cut ends of a tendon with much less tension.

Severance of the nerve to the muscle would, of course, accomplish this but the length of time required for regeneration of the nerve would render this method impractical aside from the difficulty of isolating individual muscle nerves.

Experiments dealing with the obliteration of contracture of muscles were carried out many years ago in cases of tetanus. In this condition, the continuous shortening of striated muscle (so called rigidity) is caused by the action of tetanus toxin on the spinal cord. The toxin does not have any action either acute or chronic on the muscle or any other contractile element. In 1894, Goldscheider brought about slight relaxation of the contracture in acute tetanus with cocain, and Autokratow secured a brief relaxation of local contracture by the local application of cocain. Meyer and Weiler succeeded in bringing about

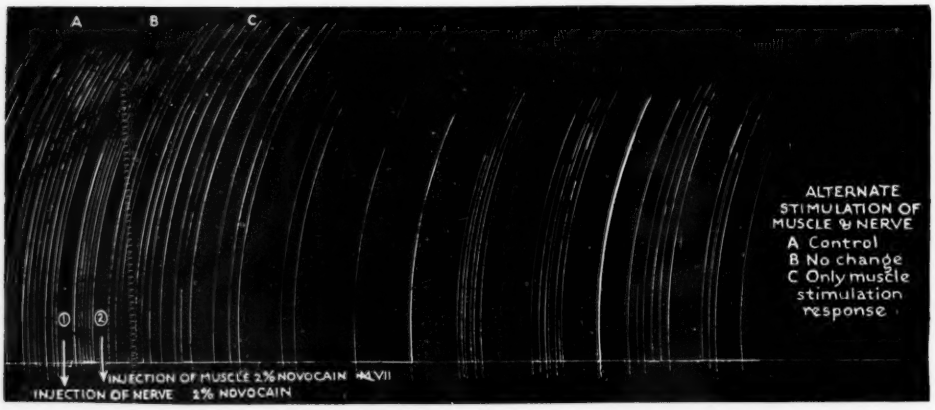

Fig. 2. Showing response of muscle to nerve stimulation following injection of nerve with novocain (2 per cent) Injection of muscle eliminates response of muscle to nerve stimulation.

a prompt relaxation of trisumus by the injection of 10 to 15 cubic centimeters of 1 per cent novocain into the bellies of the masseters. From their work, it is apparent that relaxation does occur in a muscle in primary contracture by the intramuscular injection of novocain. Froelich and Meyer verified this and in their experiments it was also shown that secondary rigidity, that is, myostatic contracture, produced in rabbits and cats was not affected by the intramuscular injection of novocain.

Liljestrand and Magnus made further studies of the effects of novocain on normal skeletal muscle. They found that in decerebrate cats rigidity of the triceps was greatly decreased by the intramuscular injection of small doses (½ to 1 cubic centimeter of 1 per cent solution) of novocain and completely abolished by the intramuscular injection of larger doses (4 to 9 cubic centimeters of 1 per cent solution).

With the use of small doses, active motility remained unchanged and on indirect faradic stimulation from the plexus, its threshold value was the same as in the non-injected muscle. Larger doses overcame the indirect stimulability of the muscle and therefore the last remnants of decerebrate rigidity and active motility. Direct faradic stimulability of the muscle was still preserved.

When the posterior roots to a foreleg were cut and rigidity brought about after that by decerebration in which the desensitized leg was involved, the intramuscular injection of small doses of novocain had no effect on the rigidity. It required larger doses of novocain which impaired the indirect stimulability of the muscle to decrease and overcome this rigidity. Thus they show that novocain in small doses injected intramuscularly paralyzes the proprioceptive sensory muscle nerves and thereby decreases the reflex decerebrate rigidity. Novocain in larger doses paralyzes the motor nerve ends in the muscle and in that way completely overcomes the rigidity as well as the reflex and indirect stimulability. The response of the muscle to direct stimulation is preserved.

Walsh made similar observations in man in a study of the tremor and rigidity in patients suffering from paralysis agitans. He found that small doses of novocain injected intramuscularly diminished and finally abolished the rigidity of the muscle injected but did not remove the indirect influence through the labyrinthine reflexes. While voluntary control of the muscle was present there developed a sensation of loss of orientation in the extremity. Walsh attributed this reaction to the removal of afferent impulses from the muscle—the proprioceptive impulses. When large doses of novocain were injected into similarly afflicted muscles, there developed a flaccidity of the muscles injected with complete loss of motor control.

TABLE I.—DURATION OF ACTION OF NOVOCAIN ON REPEATED DAILY INJECTIONS IN THE SAME MUSCLE GROUP.

No.	1 Per Cent Novocain				2 Per Cent Novocain
	1st day	2nd day	3rd day	4th day	5th day
I	2	2.5	1.5	1	2.5
II	1.5	3	2.5		
III	2	1.5	2	2	2.5
IV	3.5	2.5	2	1	2
V	2.5	3	2.5	.5	3
VI	.5	3	1.5		
VII	2	3.5	1.5	1	2.5
VIII	3	2.5	2.5		
IX	4	3.5	2	1	2.5
X	2.25	3	2.5	2.5	2.5

It appears that a gradual tolerance is developed. A 2 per cent solution may prolong the action.

TABLE II.—1 PER CENT NOVOCAIN AND ADRENALIN 1:60,000

No.	1st day	2nd day	3rd day	4th day
I	3	2.5	2.5	0.5
II	2.5	2	2	
III	1.5	2.5	1.5	1.5
IV	0.5	1.5	2	1.5
V	2.5	2	1.5	2
VI	2.5	3	2.5	1

Adrenalin added to novocain in the proportion of 1 drop to 1 dram does not appear to prolong the duration of action of novocain.

We have demonstrated the action of novocain injected intramuscularly with a muscle nerve preparation from the frog. Referring to Figure 1, alternate stimulation of the muscle directly and the nerve to the muscle results in a prompt and vigorous muscle response. Flooding the muscle belly with a 1 per cent novocain solution results in a gradually failing response of the muscle to nerve stimulation. Complete failure of response develops in about 5 minutes. Direct stimulability of the muscle was not interfered with. Injection of the nerve or bathing the nerve in a novocain solution did not diminish the response of the muscle to faradic stimulation of the nerve proximal to the injected area (Fig. 2).

Fig. 3. A, Healed severed tendon. Muscle not injected. Note relative amount of fibrous tissue necessary to fill gap. B, Healed severed tendon. Muscle injected with novocain (1 per cent) daily for 4 days showing diminished amount of fibrous tissue necessary to fill the gap. Muscles A and B are corresponding muscles of the same animal.

We may, therefore, conclude that novocain prevents the reception of nerve stimuli by the muscle but does not interfere with the power of contraction. The drug evidently acts on the motor nerve end plates in the muscle preventing the impulses from activating the muscle fibril at its point of contact with the motor nerve. Fulton, from his studies, concluded that this point of contact or receptive substance resides within the muscle nuclei.

In the living non-anæsthetized dog this action of novocain on the muscle can be demonstrated by injecting 8 to 10 cubic centimeters of a 1 per cent solution of novocain into the bellies of the extensor muscles of the paw and toes. As a control, a similar volume of normal salt solution may be injected into the corresponding muscles of the opposite foreleg. Such an animal will, in the course of 5 to 10 minutes, lose voluntary control of the paw the extensor muscles of which were injected with novocain. On attempting to walk, if the paw strikes the ground perpendicularly, the animal's foreleg will fold under with the dorsum of the paw resting on the ground. The opposite foreleg injected with normal saline will not show a similar response. This action of novocain will last for a variable time from 30 minutes to 4 hours. In some animals a 2 per cent solution is more effective than a 1 per cent solution (Table I).

In a limited number of experiments, it was found that the addition of adrenalin to the novocain solution did not markedly influence the duration of paralysis but this point is still uncertain since the duration of action varies so much that it is difficult to establish

TABLE III.—EFFECT OF REPEATED INJECTIONS

No.	Duration, days	Side injected cm.	Side not injected cm.	Amt. of solution, c.cm.	Days injected	No. each day
I	39	1.2	1.4	8	0	0
II	21	1.0	.9	6	1	1
III	41	1.8	1.8	10	1	1
IV	34	1.6	1.4	8	2	1
V	48	.4	.9	6	4	1
VI	48	.5	.8	5	4	1
VII	38	.4	.7	6	4	1
VIII	60	.6	1.0	8	5	1
IX	57	1.0	1.5	8	5	1
X	71	.7	1.1	6	4	1
XI	40	.8	1.4	8	4	2
XII	36	.6	1.3	8	4	2
XIII	41	.6	1.5	6	4	2
XIV	36	.8	1.6	8	4	1
XV	46	.7	1.3	8	5	2
XVI	31	.3	.9	5	5	2
XVII	36	.3	.7	6	5	2
XVIII	14	1.0	1.5	8	5	2
XIX	39	.8	1.2	8	4	2
XX	11	1.2	1.2	8	2	1

Average retraction non-injected muscles..... 1.2
Average retraction injected muscles..... .7

a basis for comparison (Table II). The reason for this variability of the action lies perhaps in the intact blood supply to the muscle.

In another series of dogs, we directed our attention to the effects produced by repeated injections of novocain into the belly of a muscle the tendon of which had been severed. It was found that repeated injections of novocain for 4 to 5 days definitely reduced the amount of retraction as shown in Table III. In our experimental animals, this diminution in the extent of the retraction lessened the amount of fibrous tissue necessary to fill the gap produced in the tendons, hence, healing took place correspondingly sooner (Fig. 3).

Microscopic examination of the muscle tissue after repeated injections of novocain reveals no appreciable change from the normal.

DEDUCTIONS

It would seem from our experimental work that the injection of novocain into the muscle belly definitely lessens the retraction of a severed tendon. Since the voluntary activities of an unanæsthetized experimental animal cannot be controlled, the data obtained cannot well be applied to man in whom it would be an easy matter to maintain voluntary inactivity. The duration of relaxation following injection may be largely dependent upon the volume of blood flow through the muscle belly per unit of time. Muscle activity produces enormous changes in the circulation through muscles. Krough states that during activity the total capacity of the vascular bed of a muscle may be increased from 0.02 per cent to 15 per cent of the total volume of the muscle. Thus it may be explained how inactivity of an extremity might prolong the duration of the action of novocain while muscular activity would probably shorten the action. In each case it will always be difficult to judge the time necessary to establish union of sufficient strength to permit the discontinuance of efforts at muscular relaxation. We feel that the clearing up of these points will greatly facilitate the clinical application of the suggested use of novocain in tendon repair.

CONCLUSIONS

From the present study, we are able to conclude the following:

1. Novocain injected intramuscularly definitely removes the influence of the nervous system on the muscle injected.

2. In the unanæsthetized dog, the duration of this elimination of nerve influence following a single injection lasts a variable period of time from 30 minutes to 4 hours.

3. Repeated injections with novocain of a muscle the tendon of which has been severed is sufficient to induce continuous muscular relaxation by eliminating the primary hypertonic contracture.

4. The decrease of tendon retraction permits an earlier healing by decreasing the amount of fibrous tissue which is necessary to fill in the gap which is produced in the severed tendon.

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THE EFFECT OF LIGATING THE TAIL OF THE PANCREAS IN JUVENILE DIABETES[1]

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In previous animal experiments, carried out following the original suggestion of Mansfeld, it was found that when the tail of the pancreas was tied off or completely isolated in the dog, a series of important changes resulted. The isolated tail ceased to function as an organ of external secretion, as the acini degenerated and a marked sclerosis and atrophy of the tail took place (5). The islands seemed to survive this sclerotic process and even showed hyperplasia and hypertrophy. Moreover, this hyperregeneration was encountered in the unligated head and body of the pancreas (7). My co-workers and I could also demonstrate an increase in carbohydrate utilization in the normal dog, following a ligation of the tail of the pancreas (9). The increase in sugar tolerance was noticeable between the third and fourth months after the operation but did not persist to any extent, over a period of a year. Causes for the return of the sugar tolerance to normal in the normal dog are now being investigated.

Whether such suggestive experimental findings could be applied in human diabetes was doubtful. In a preliminary report on the first diabetic child operated on, Wilder and I pointed out (8) that hypertrophy of the islets might not take place in human diabetes, and, even if it did, the new islets might succumb to the same deletary influence that inhibited the efficient function of the original cells. Yet the following clinical facts seemed to make a clinical trial promising. First, the great regenerative power of the human islet cells is seen following destruction of pancreatic tissue in acute pancreas necrosis or carcinoma of the pancreas. While temporary glycosuria may occur in these diseases, the loss of tissue is readily compensated for and true diabetes mellitus does not frequently result. Such examples from the literature and our own observations have been recorded elsewhere (6). Second, the pancreas of the diabetic also shows signs of regeneration. Particularly Weichselbaum and Cecil (3) pointed out the occurrence of hypertrophic islets in diabetes. Other observations are cited in a previous article (6) and an excellent summary together with a number of new observations on islet regeneration is given by Shields Warren.

As we had experimental evidence which suggested a possible increase in islet function and as numerous postmortem observations are on record regarding the regenerative power of the diabetic pancreas, we felt that it was worth while to try to determine the effect of ligature of the tail of the pancreas in patients suffering with diabetes.

INDICATIONS

Juvenile diabetes seemed theoretically the type of diabetes in which an attempt to increase sugar tolerance would be most promising. The regenerative power of the islets in children is obviously greater than in adults;

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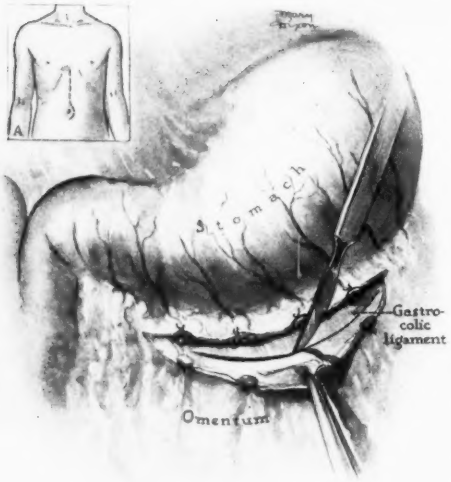

Fig. 1. *A*, Midline incision, encircling the navel to the left. An incision is made to the left of the midline through the great omentum and gastrocolic ligament, thus exposing the omental bursa.

for secondary changes in the vascular system, particularly in the blood supply of the islets, have not yet taken place. In children, the islets themselves do not show morphological changes, although, as emphasized by Warren, in many adult patients with diabetes, the islets are singularly free of degenerative processes.

Furthermore, the juvenile type of diabetes is usually severe and difficult to manage. While it is true, that the advent of insulin has reduced the mortality in juvenile diabetes from 90 per cent to around 10 per cent, and while according to recent figures of Wilder and Allen the mortality in the year 1929 at the Mayo Clinic was only 1.2 per cent, it must be remembered that there still remains many cases of juvenile diabetes in which the diabetes is inadequately controlled and the children afflicted die of diabetic coma. When the operation of ligating the pancreas is suggested, it must be postulated that the operative risk is not greater than the mortality percentage of the diabetic child *per se*, and that the diabetes itself will not be aggravated. Both these postulates can be easily fulfilled by this surgical attempt.

Naturally not all diabetic children are suitable for such a trial. In mild cases, when the child's tolerance is fairly stable and the caloric intake is high enough for normal development without too much insulin, the patients are doing well under medical management. Joslin feels that this new generation of juvenile diabetics, who grew up under continuous dietary and insulin control, are offering the best example for the vast importance of insulin. It would not seem justifiable, with our present knowledge of the effects of this operation, to advise surgery to this group.

It is then in the severe type of juvenile diabetes with unstable tolerance, with frequent occurrence of acidosis and coma at the slightest infection, with unexpected insulin reactions, that this operation might be tried. But here again the time of operation must be carefully selected. It has been stated by Wilder (18) that juvenile diabetes usually starts with unusual severity and that under adequate dietary and insulin control, the tolerance gradually improves and becomes stable. If one is to evaluate the result of this operation, the child must have been diabetic for at least 2 years and must have been practically sugar free for at least 6 months, with a stable or slightly improving tolerance.[1] On the other hand, patients whose diabetes dates back 8 or 10 years, much of which time they have not been properly controlled, may show too many secondary changes to permit great improvement from operation.

PREPARATION OF PATIENT

As in any other operation on diabetics, the patient must be sugar free and should have no diacetic acid in the urine. It has also seemed advisable to administer for the last 3 days from 120 to 150 grams of carbohydrate in the diet, so that sufficient glycogen is stored in the liver. An enema is given only if the patient has not had a bowel movement on the day before the operation. A light sedative, one or two tablets of allonal, is prescribed for the night before the operation, and the dose repeated 2 hours before the operation. The morning dose of insulin is omitted, and a glass

[1] Only recently have we postponed the operation on a severe diabetic child who did not seem adequately controlled. It is known that proper control will increase their tolerance to some extent.

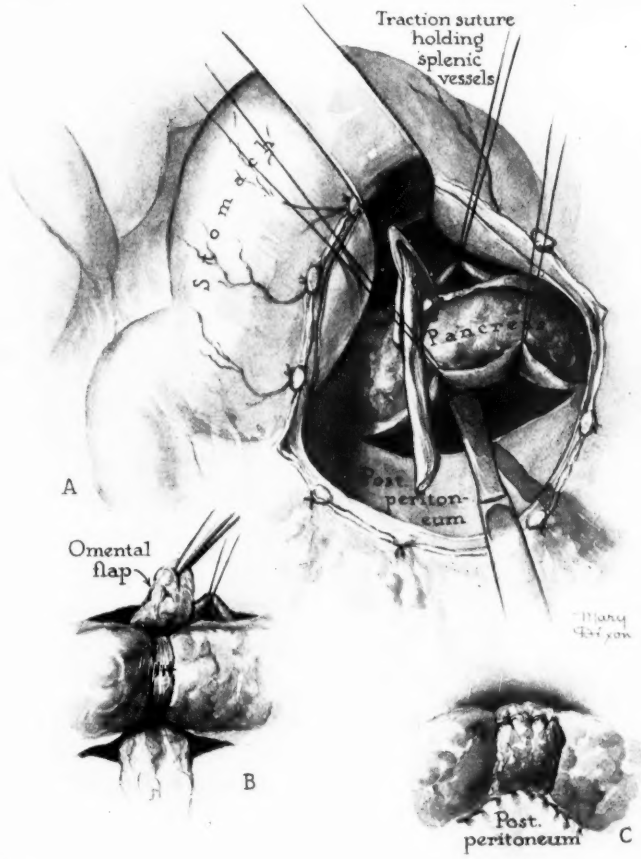

Fig. 2. *A*, A wide flexible retractor lifts and everts the stomach. The posterior peritoneum is incised parallel and slightly below the lower margin of the pancreas. The splenic vessels have been dissected off the posterior surface of the gland and retracted by gentle traction. A strip of fascia lata is threaded into the eye of a flexible director, which is passed behind the gland. *B*, The strip of fascia lata has been snugly fastened around the pancreas with interrupted and interlocking sutures of fine black silk. A flap of omentum is used to protect the fascial ligature. *C*, The lower lip of the posterior peritoneum is brought up to cover all raw surfaces and close the retroperitoneal space.

of orange juice is given at least 2 hours before operation. Half an hour before the operation, a small dose of pantopon ($\frac{1}{3}$ grain to $\frac{1}{4}$ grain) and atropine $\frac{1}{120}$ grain are injected under the skin.

ANÆSTHESIA

While I use spinal anæsthesia as much as possible in diabetics, the field of operation lies so high and the traction on the vagal fibers produces so much nausea. that its use has not been considered. Avertin seemed to be equally unsuitable because of the marked acidosis that it produced. Under a light nitrous oxide anæsthesia, a typical abdominal field block is produced with 80 to 100 cubic centimeters of a $\frac{1}{2}$ per cent novocain. Three drops of a 1:1,000 epinephrine solution are added to

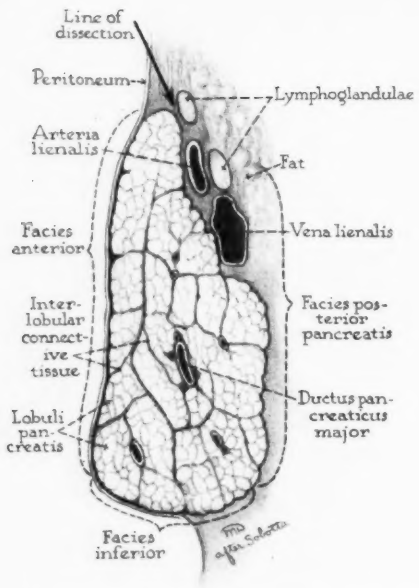

Fig. 3. Transverse section of the pancreas at the site of ligature. Note the splenic vessels in a groove behind the pancreas. Enlargement and inflammatory reaction of the superior pancreatic lymph glands may interfere with a clean line of cleavage.

every ounce of the solution. Before the peritoneum is opened, it is copiously infiltrated again, and after the incision is made, about 10 cubic centimeters are injected to the right and left of the incision from the inside to permit a painless insertion of an automatic retractor. Up to this stage, the nitrous oxide anæsthesia can be kept very light. Before any of the viscera are disturbed, the greater and lesser omentum are lightly infiltrated with novocain. A reverse Trendelenburg position is helpful to keep the intestines out of the way and to permit the lesser curvature of the stomach to appear at the upper angle of the incision. After the stomach has been reflected upward and the body of the pancreas appears behind the glistening posterior peritoneum, some novocain is again deposited at the upper and lower margin of the pancreas. At the upper margin of the pancreas, the needle may be inserted deeper, to the right of the pulsating aorta and to the left of the palpable vena cava, thus producing a typical anterior splanchnic anæsthesia (4). However, if the patient strains at this point, and the exposure is not satisfactory, an ounce or two of ether will obviate the performance of the splanchnic block.

After the ligation of the tail has been accomplished, the nitrous oxide anæsthesia and the abdominal field block will permit an easy closure, and the ether, if used at all, may be discontinued. The small quantity of ether may prove of great help to facilitate exposure and shorten the duration of the operation. It certainly is less harmful than a valiant struggle with the protruding intestines.

TECHNIQUE OF THE OPERATION

A midline incision is made between ensiform cartilage to just above the umbilicus, encircling it to the left (Fig. 1, *A*). If necessary, the incision may be continued further down, or, as in the first patient, a transverse incision can be added through the left rectus, such as Kocher, Czerny, and others have employed for difficult gall-bladder exposures on the right side (1). In the second patient, however, the midline incision, as shown in the illustration, provided the necessary exposure. The incision is made through the linea alba. Just before the peritoneum is opened, the patient is brought into a reverse Trendelenburg position, which helps to remove the coils of small intestines from the field of operation. The gall-bladder pad below the dorsal spine is elevated. An abdominal retractor is inserted and the midportion of the stomach, particularly the greater curvature is exposed. Next an incision is made to the left of the midline through the greater omentum and gastrocolic ligament, thus freeing the greater curvature as in a partial gastrectomy (Fig. 1). A curved flexible probe, threaded with catgut picks up small amounts of tissue, and after a double ligature, the tissue between is cut. After the stomach has been freed satisfactorily, a wide flexible retractor is used to lift and evert the stomach, thus exposing the omental bursa and the posterior peritoneum. In the posterior peritoneum, a small incision, about 3 centimeters long, is made parallel and slightly below the lower margin of the pancreas (Fig. 2, *A*). Small artery forceps or traction sutures now may be used to exert gentle pull on the

posterior peritoneum and, with it, on the pancreas itself. This facilitates the exposure and dissection of the splenic vessels, which run in a groove behind the body of the pancreas surrounded by lymph glands (Fig. 3). While the artery may be easily recognized by its pulsation and by its appearance at the upper margin of the tail of the pancreas, the vein must be dissected off bluntly and under the control of the eye, the gland being everted more and more with the traction sutures. When the splenic vessels are dissected off the posterior surface of the pancreas, the most delicate part of the operation has been completed. It is well to remember that as a rare anomaly, the splenic vessels may run in front instead of behind the pancreas (15). The vessels should be freed only for a short distance, so that none of the short branches, entering the gland at right angles, are injured. While it is desirable to tie off a large portion of the gland, care must be exercised to remain to the left of the midline, in order to avoid the superior mesenteric vessels.

A strip of fascia lata 1 centimeter wide and about 10 to 12 centimeters long, is now removed. I have preferred to use fascia lata, instead of the anterior rectus sheath, as the removal of the latter may weaken the abdominal wall and cause bleeding in the muscle. This strip is threaded into the eye of a flexible director passed behind the gland and snugly sutured around it (Fig. 2, *B*). Interrupted and interlocking U sutures of fine black silk were used. In future operations it would probably be well to use McNealy's method, by which he produces partial occlusion of the arteries (14). The amount of constriction used in the ligature of the pancreas is obviously important. It should not be so tight as to cut through, and if tied too loosely it will not occlude the duct. It must be remembered, however, that the œdema following the ligature will increase the obstruction, and that if one may judge from the animal experiments, a fibrous constriction ring will form around the ligature. To ensure better vascularization of the fascia and to wall off a possible exudate around the constriction, a flap of omentum is thrown around the ligature (Fig. 2, *B*). Finally, the lower lip of the posterior peritoneum is used to cover any raw surface that might later give rise to adhesions (Fig. 2, *C*). The gap in the gastrocolic ligament is carefully closed with interrupted sutures. No attempt is made to drain the omental bursa through a lumbar stab wound, although one might feel tempted to do so. This probably should have been done in the first patient, in whom the gland was actually severed with a high frequency cautery. However, the ligature seemed safer and it had proved to be just as effective in the animal experiment; moreover, the clean peritonealized surfaces could only be harmed by drainage. Besides the drainage of an œdema possibly ensuing in the omental bursa hardly seemed feasible.

The abdominal wall is closed with a continuous plain catgut suture of the peritoneum and interrupted chromic catgut sutures of the linea alba. Three or four stay sutures are inserted through skin and muscle, the skin is sutured with interrupted fine silkworm sutures, and the stay sutures are snugly tied over a roll of gauze. A light mastisol dressing is applied to keep the gauze in place, and an abdominal binder is applied snugly over it. Tight adhesive dressings are avoided.

POSTOPERATIVE MANAGEMENT

Because of the extensive mobilization of the stomach and because of the well known clinical fact that exudates in the omental bursa produce gastric and colonic atony, attention must be drawn to prevent or overcome paralytic ileus. Nothing is administered orally for the first 48 or even 72 hours. If the patient is nauseated or is still vomiting after 24 hours, permanent gastric drainage is instituted with a Rehfuss tube, and the stomach contents are aspirated every 2 hours. This procedure became necessary in the first case, while in the second case no gastric dilatation occurred. One hundred grams of dextrose are supplied daily in the form of subcutaneous or intravenous drips. Five per cent dextrose solution is used in the subcutaneous drip and 1,000 cubic centimeters is given in about 5 hours, through fine needles. Thus very little discomfort is experienced. If the subcutaneous route is used entirely, 2,000 cubic centimeters will supply the 100 grams, and another thousand

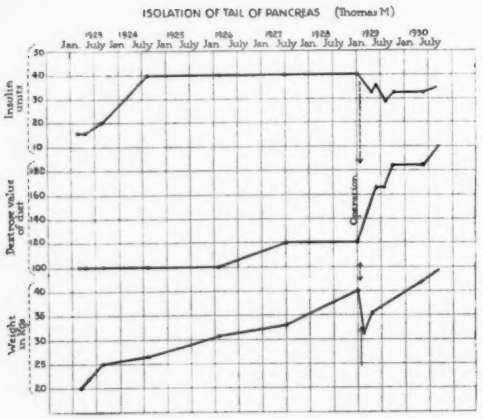
ISOLATION OF TAIL OF PANCREAS (Thomas M.)
1923 1924 1925 1926 1927 1928 1929 1930
Jan. July Jan. July Jan. July Jan. July Jan. July Jan. July Jan. July Jan. July
Insulin units
Dextrose value of diet
Operation
Weight in kgs.

Chart 1. Graph illustrating pre-operative and post-operative values of insulin requirement, dextrose value of diet, and weight in the case of Thomas M., aged 13 years, at time of operation.

cubic centimeters of Ringer's solution will maintain the mineral balance. It may be difficult to keep up this method of administration for 3 days and therefore the intravenous route is resorted to. In the intravenous route 10 per cent solutions are used with the Hendon needle (10), the normal rate of utilization, namely one gram per kilogram per hour never being exceeded. It should take an hour to inject 50 grams of dextrose in a child weighing 50 kilograms. No dextrose is given rectally, because probably very little is absorbed and it causes increased colonic distention.

While these children are not totally diabetic, they may be considered as such following the insult of the operation. The 100 grams of dextrose must be covered at least by 45 units of insulin, equally distributed every 3 hours. However, the insulin requirement of diabetics following operation very often exceeds the theoretical requirements. In older diabetics, in whom amputation has been done for gangrene, in spite of the absence of general anæsthesia and infection, the amount of insulin required to keep them sugar free may be very high for the first days. If the patient is able to void on the first day, the urine is examined every 4 hours and insulin is given according to the diagram outlined by McKittrick and Root. If specimens of urine are not available, microscopic blood sugar determinations are made three times a day. These are specially valuable in helping to determine the overdosage of insulin, which must usually be reduced a few days after operation. It is very important to avoid excessive high blood sugars after the operation as a proper control will insure undisturbed wound healing. A 10 cubic centimeter syringe and a 20 cubic centimeter ampule of 50 per cent dextrose are kept ready to use in case of insulin reactions.

Following the first 2 and not later than 3 days, a fluid diet, consisting of orange juice and milk is started, the carbohydrate intake of 100 grams being maintained. A low enema is given with 1 ounce of glycerin to 3 ounces of water on the third postoperative day. If a bowel movement has taken place and the abdomen is not distended, gradually a soft diabetic diet and then a full diet is given. At the end of the first week, the patient should be back on the pre-operative diet. The insulin requirement has been somewhat higher in both cases, probably owing to the œdema of the pancreas at that time.

The patient is made to sit up the evening of the operation, encouraged to take a deep breath at frequent intervals, and, if no complications set in, may be in a wheelchair on the fifth day. Stitches are removed on the tenth day. If primary union took place, there is no need to keep the patient in the hospital more than 14 days.

Obviously the postoperative diabetic management must be in the same expert hands as before the operation. It is particularly important to have the diabetes fully controlled after the operation, as the presumable hypertrophy and hyperplasia of the islet cells could be easily frustrated in the poorly controlled case. It is best to have the children test their own urine three times a day and to give themselves a little more or less insulin, according to the daily requirement. In both of our cases operated upon, insulin reactions began to occur about the fourth month following the operation. This calls for a gradual reduction of insulin. If the patients have been made to maintain throughout the entire period their original, pre-operative diet (a requirement, which for certain reasons our cases did not entirely fulfill), the reduction of insulin will

numerically express the increase in tolerance. That infections or injuries will influence this gain in tolerance was very obvious in both cases.

RESULTS

CASE 1. Detailed history of this case was given in a previous communication (8). The diabetes had been present previous to operation for 8 years. Patient had been under dietary and later insulin management, supervised by Dr. Russell M. Wilder at the Mayo Clinic for 6 years. At first his tolerance grew worse steadily. For the last 2 years before operation the patient had been taking 40 units of insulin, the dextrose value of the diet being 120 (carbohydrates 76, protein 50, fat 150).

The operation was performed on January 21, 1929. The small, definitely hypoplastic tail was divided with a high frequency cautery. The patient had a stormy convalescence during which time drainage of the omental bursa had to be instituted twice. He was discharged from the hospital on March 16, 1929, on the original diet, with 45 units of insulin, 5 units more than before the operation. For the next 3 months, the insulin requirement remained steadily between 40 and 38 units. From April 26 on, insulin reactions began to occur after the morning dose, which prompted a gradual reduction. On May 9, 1929, 110 days after the operation the lowest level of 25 units was reached. From then on the insulin had to be increased to 35 to 39 units, a stitch abscess of the abdominal incision having developed. On June 4, the boy's diet was increased, as he still weighed 8 pounds less than before the operation. The new diet consisted of carbohydrates 102 grams, protein 75 grams, and fat 161 grams, a dextrose value of 166. On June 18, 1929, the insulin dose was 39 units, on August 2, 29 units. On May 31, 1930, 17 months after the operation the patient weighed 5 pounds more than before the operation, had grown an inch and a half, took 63 grams more dextrose, with 8 units less of insulin (Chart 1). In September, 1930, 20 months after the operation the patient was on a diet of carbohydrates 134, protein 88, fat 162, dextrose value of 200 and 37 units of insulin, a gain of 80 grams of tolerance since the operation.[1]

A severe diabetic child whose previous diabetic history is well known, and who was stabilized for 2 years before operation, is at the present writing, growing and gaining weight normally, with a slightly diminished dose of insulin, but utilizing 80 grams of additional dextrose. This definite increase in tolerance occurred in a patient who for 6 years had gradually lost tolerance and who for the last 2 years previous to operation had not shown any change at all.

CASE 2. Detailed history was given elsewhere (6). He had been in a tuberculosis sanitarium with tuberculous cervical lymph glands for over 3 years, being discharged as well at the age of 10. At the age of 14, 2 years previous to operation, it was first noticed by

[1] On June 1, 1931, 28 months after the operation, the gain in tolerance still persists. The insulin has been reduced to 30 units.

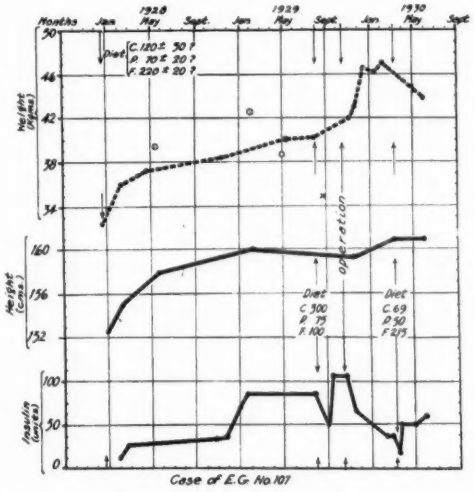

Chart 2. Graph illustrating pre-operative and post-operative values of weight, height, diet, and insulin requirement in the case of Eugene G., aged 16 years, at time of operation.

the parents that he passed a great deal of urine and had lost weight. He was admitted a few days later to the Billings Hospital in coma. In November, 1927, he was discharged on a diet of carbohydrates 90, protein 65, fat 216, 2,600 calories, without insulin. Between this date and the date of operation, October 15, 1929, he had 9 further admissions to the Billings Hospital. More and more insulin had to be given, but control was very difficult. He had several respiratory infections, an emergency appendectomy, all of which affected his tolerance. He had also been very careless about his diet and ignored it several times. Finally on his tenth admission, as he had done poorly on a low carbohydrate, high fat diet, and continued to pass sugar on a diet of carbohydrates 120, proteins 85, fats 200, with 80 units of insulin, it was considered advisable to try him on a high carbohydrate, low fat intake. This resulted, at least temporarily in a marked decrease in the insulin requirement. On his discharge August 30, 1929, his diet consisted of carbohydrates 300, protein 75, fat 100, dextrose value of 354 with 45 units of insulin.

On October 1, 1929, the patient was admitted to the Wesley Memorial Hospital under the diabetic management of Dr. William H. Holmes (Case No. 147,279 W.M.H.). He was operated upon on October 18, 1929, during the Clinical Congress of the American College of Surgeons. The pre-operative diet was carbohydrates 300, protein 75, fat 100, and insulin 35-35-35. The operation was performed as described in this paper. The patient made an uneventful recovery with primary union of the incision. He left the hospital on the fourteenth day. A month later on the same diet and 60 units of insulin he

weighed 42 kilograms (+3 kilograms, since the operation). Two months after the operation, the patient had gained another 4 kilograms. Four months after the operation he was getting severe insulin reactions, so that the dosage had to be reduced to 40 units a day. On February 25, 1930, he was readmitted to Billings Hospital because of an upper respiratory infection. Temperature rose to 101.1 degrees F. He required now 70 units of insulin but could soon be reduced to 45–50 units.

On March 9, 1930, he was taken off the high carbohydrate diet and given carbohydrates 59, protein 50, fat 215, a glucose value of 120. The insulin requirement fell to 18 units. The next week the insulin had to be raised and on March 23, a chickenpox developed with high temperature and extensive eruption. The insulin requirement rose to 50 units and his tolerance was upset for several months. On June 20, 1930, Miss Florence Smith, chief dietitian of the Billings Hospital, reported the following data. Diet carbohydrates 139, protein 75, fat 209, a dextrose value of 203, with 55 units of insulin. This was 3 months after the chickenpox infection started, but the tolerance seemed to increase slowly (Chart 2).

On October 15, 1930, a year after the operation, patient was still taking the same diet and insulin, although occasionally, when under rigid control in the hospital, it was possible to reduce the insulin to 35 units. This patient's tolerance is not stable, and during the school year is always lower than in the diabetic camp.[1]

A diabetic child, whose disease is known to have been present for at least 2 years, and whose tolerance was rapidly growing worse, was operated on. The child made a rapid recovery. Four months after the operation, a reduction of insulin could take place. Five months after the operation, the high carbohydrate low fat diet was changed to a low carbohydrate, high fat diet with a large reduction of insulin. A little later, a chickenpox infection upset the sugar tolerance, from which the patient, 3 months after this infection and 11 months after the operation, is gradually recovering.

In a disease of life's duration, with spontaneous fluctuations, with such sensitive response to infections and emotional influences, we can not be too cautious in interpreting results. It is true that the result in either of the two cases operated upon is not a fair example of what can be accomplished with the method. In the first patient, the presence of a small, hypoplastic tail of the pancreas prevented the isolation of a large enough portion of the gland. In the second patient, as pointed out by Wilder, the high carbohydrate diet, which has been given according to Porges and others to stimulate insulin-production, might have been injurious and that better results could have been expected if the pancreas had been allowed to rest rather than being stimulated in the period when the islets were undergoing hypertrophy. Insufficient time has elapsed in both cases to predict the ultimate result.

Nevertheless, the animal experiments and the observations in the two clinical cases show striking parallelism. The increase in tolerance is gradual, occurs around the fourth month, and does not persist at its highest level but gradually diminishes. The assumption that an islet hypertrophy takes place in the diabetic child could not be verified up to date histologically, but seems very probable.

This regeneration or even superregeneration of islets does not strike at the real cause of diabetes. Unless we will be able to protect these islets from injurious effects of nervous or hormonal origin, the new islets will become exhausted like the original ones. If Epstein's theory of tryptic action on the islets were true, the exclusion of external secretion from the tail would be particularly significant. If some other insulin-inactivating agent were at work, then a surgical attempt of islet regeneration *alone* would not lead to permanent results.

So long as the cause of diabetes is unknown, a surgical attempt to improve diabetes can only have the following aims:

1. *A stabilization of tolerance*, whereby the children are more easily controlled, less subject to acidosis and coma. In other words, to transform the unstable juvenile diabetes into a stable type of the older patient. Both cases seem to show this effect very definitely.

2. *A reduction or possible abolition of insulin*, on a liberal diet. If better utilization of sugar would take place on the same or less amount of insulin, the better development of these children might be brought about. This second requirement has not yet been entirely fulfilled. There is enough suggestion, however, in the first cases to warrant further trial.

A report on other cases, with a further report on the first two children will be made at a later date.

[1] On June 1, 1931, 20 months after operation, patient's status is the following. Diet, carbohydrates 140, proteins 75, fat 200, a dextrose value of 200, calories 2,700 with 60 units of insulin. He is unable to gain weight on this high caloric diet and has some upper abdominal pain. It is possible that the retroperitoneal tuberculous lymph glands seen at operation are responsible for his present condition. An exploration is now under discussion.

SUMMARY

In two carefully selected cases of juvenile diabetes the tail of the pancreas has been isolated on the basis of animal experiments, which show hypertrophy and hyperplasia of the islets and increased carbohydrate tolerance after such an operation. Longer period of observation, and further trial on other cases promise a better evaluation of such attempts.

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MESENTERIC VASCULAR OCCLUSION[1]

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OCCLUSION of the mesenteric vessels is generally regarded as a comparatively rare condition; however, it occurs often enough to require consideration whenever obscure acute abdominal lesions are encountered. It is the severity of the condition and not its frequency which makes it significant. Owing to the difficulty in its diagnosis and the usual conception of its rarity, many cases undoubtedly remain unrecognized clinically, and death is ascribed to postoperative ileus, peritonitis, and so forth.

The first case of mesenteric vascular occlusion was recognized and reported by Tiedemann in 1843, and an extensive pathological study of the affection was made by Virchow in 1847. The latter described closure of the superior mesenteric artery, resulting in an intestinal infarct. Seven years later, he described a similar case. The clinical aspects of the subject were not accorded much consideration, however, until they were emphasized by Kussmaul and Gerhardt in 1863. Thereafter reports of cases were recorded by many writers. In a comprehensive monograph in 1913, Trotter analyzed the 360 cases already in the literature and added 6 new cases of his own. From a careful study of these cases, he was able to draw valuable conclusions. His statistics show that a pre-operative diagnosis was made in only thirteen cases. From 1916 to 1918 various reports were published (1, 2, 3, 4, 5, 6, 8, 9, 10, 11).

REVIEW OF CASES

Thirty-six cases of mesenteric vascular occlusion, in which necropsy was performed, are presented as a basis for this paper (Tables I and II). These may be classified as follows: arterial, 14 cases (39 per cent); venous, 16 cases (44 per cent); and co-existent venous and arterial, 6 cases (17 per cent). These percentages are in rather close agreement with the relative frequency as found by other authors.

Arterial occlusion may be due either to thrombosis or embolism, or a combination of both, and when the closure is complete in either of the superior or inferior mesenteric arteries, the resulting injury is of a serious nature. This is due to the fact, as has been explained by Klein, that the mesenteric arteries are end arteries functionally but not anatomically. Incomplete closure of the vessels is not so serious and is probably the origin of symptoms described as mesenteric intermittent claudication. This narrowing and sclerosis of the arteries of the mesentery give rise to attacks of nausea, vomiting, flatulence, and abdominal pain, many times finally resulting in complete occlusion due to the formation of thrombi. Case 7 of this series illustrates the sequence of events in cases in which incomplete closure of the vessels takes place.

Intestinal infarction resulted in 12 of the 14 cases of occlusion of the superior mesenteric artery. No case of occlusion of the inferior mesenteric artery was encountered. Arterial occlusion from thrombosis was found to be slightly more common than from embolism; the number of cases of each was, respectively, 5 and 4. Three of the 4 cases of embolism resulted from cardiac thrombi and 1 from a valvular thrombus. Periarteritis was present in 3 of the 5 cases of thrombosis, and arteriosclerosis in 2. The 5 remaining cases of arterial occlusion are of doubtful nature, although a mural thrombus may have been present and overlooked in Cases 11 and 12. In Case 13 a severe septic process in the genito-urinary tract may have been a factor, as this could well be a focus of infection for mesenteric arterial thrombosis. In the 2 remaining cases, pathological changes in the cardiovascular system were not recorded. Arterial occlusion did not result in intestinal changes in 2 cases. In Case 11 the short time between the occurrence of the mesenteric embolism and of the cerebral hæmorrhage probably accounts for the absence of infarction, and in Case 4 the

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onset of coronary thrombosis resulted in death before intestinal changes from occlusion of the superior mesenteric artery could occur.

Nine of the 16 cases of venous occlusion in this series were primary or ascending, and 5, secondary or descending; the 2 remaining were of rather indeterminable type. In the primary type of case, the cause most often lies in changes in the intestinal tract, which permit the entrance of bacteria. Inflammation of the appendix was responsible in 5 cases; it was subacute in Case 15, and gangrenous in Cases 16, 17, 18, and 19, indicating that the more severe the appendiceal condition, the more likely mesenteric thrombosis is to follow. Thus, of 6 cases in which the gastrointestinal tract was responsible for the vascular condition, the appendix was the source of it in 5. In the remaining case (Case 20), severe enteritis was probably the initiator of the venous thrombosis. In Case 26, the presence of numerous suppurating decubitus ulcers was the probable source of mesenteric phlebitis, which eventually resulted in thrombosis. Possibly involvement of the mesentery by the malignant condition in the pelvis could be a factor in closure of these vessels. Miscellaneous causes were noted in the 3 other cases of primary thrombosis.

In 4 of the 7 cases of descending thrombosis of the mesenteric veins, hepatic disease was present: portal cirrhosis (Case 24), multiple hepatic abscess due to escherichia coli (Case 23), localized hepatitis following a tear in the liver (Case 22), and extreme fatty degeneration of the liver (Case 21). The 3 remaining cases resulted from miscellaneous causes.

It may be noted that of all the cases of venous thrombosis, 31 per cent followed appendicitis and 25 per cent were associated with disease of the liver.

Of the 16 cases of venous occlusion in this series, intestinal infarction occurred in 13 (81 per cent). Of these 13 cases the main trunk alone was involved in 2, the tributaries alone in 3, and both the main trunk and tributaries in 8. In the 3 cases in which there was no intestinal injury, the main trunk alone was involved. This constitutes evidence in favor of Reich's opinion that infarction occurs only when thrombosis has extended into the tributaries of the vein and has reached the intestinal wall, because branches which are free can open into the main vessels above or below the limits of the clot which the main vessels contain.

TABLE I.—CLASSIFICATION OF CASES

	Cases
Arterial occlusion	
Embolism	
From mural cardiac thrombus	4
From valvular thrombus	1
Thrombosis	
Mesenteric arteriosclerosis	2
Arteritis	3
Unknown or doubtful etiology	4
Venous occlusion (thrombosis)	
Primary or ascending	
From appendicitis	5
From enteritis	1
Secondary or descending	
Associated with diseases of the liver	4
Doubtful whether ascending or descending	6
Combined arterial and venous occlusion	
Following intestinal obstruction	2
Miscellaneous etiology	4

Six cases of co-existent occlusion of the arteries and veins are reported. In 2 of these the patients were aged, and attempts at surgical relief of intestinal obstruction preceded the onset of the thrombosis. The significance of sclerosis of the mesenteric vessels is undoubted, although traumatization of tissue, sepsis, and stasis may have been the precipitating factors. Other associated conditions found were metastatic carcinoma of the mesenteric nodes from primary rectal lesions, splenic abscess, and so forth. In 2 cases definite etiology could not be ascertained.

A review of the literature regarding experimental production of mesenteric vascular occlusion indicates that ligation of the superior artery at its origin, or at one of its primary branches, results in infarction in the region of intestine supplied by the occluded vessel. Intestinal injury usually does not result from a ligature applied distal to the anastomotic arches. Severing of the mesentery is without effect unless more than 3 centimeters is cut away, and when the omentum is wrapped around the intestine from which the blood supply has been ligated, gangrene may or may not develop. Ligature of the mesenteric veins is not always followed by infarction, although this is more likely to be the result than ligature

TABLE II.—ABSTRACT OF CASES

Case	Age Years, Sex	Clinical history and observation	Observations at necropsy	Comment
1	56 M	Acute onset of severe abdominal pain followed by shock, melena, vomiting, and rapid pulse; soft indefinite tumor palpable in lower left quadrant of abdomen; laparotomy 48 hours after onset, and death 24 hours later	Heart characteristic of hypertension with mural thrombosis of left ventricle; 1,000 c.cm. bloody ascitic fluid; infarction of third part of duodenum, the jejunum, ileum, and colon to splenic flexure; superior mesenteric artery occluded at origin by embolus and thrombus 3 cm. long	Origin of embolus from mural cardiac thrombus.
2	64 M	Onset sudden with hæmatemesis and passage of foul red urine; this followed by abdominal distention and death 48 hours later; patient had had occasional attacks of cardiac pain for 15 years	Heart characteristic of hypertension with coronary sclerosis, myocardial scar, and mural thrombus in left ventricle; infarction of last 45 cm. of ileum and local peritonitis with terminal portions of corresponding arteries occluded by thrombi	Origin of embolus similar to Case 1.
3	58 M	Sudden attack of severe abdominal pain while being treated for extensive seborrhœic dermatitis; soon followed by vomiting, fall in temperature, rise in pulse, distention of abdomen, and shock; death 5 days after onset	Coronary sclerosis with mural thrombosis of left ventricle; two infarcted areas in jejunum, one 20 cm. and the other 15 cm. in length with occlusion by thrombi of corresponding arteries and veins	Origin of arterial embolus similar to Case 1; venous thrombus secondary to intestinal infarct.
4	67 M	Patient admitted to hospital in shock; had had severe precordial pain, severe dyspnœa, and cyanosis for several hours; death 30 minutes after admission	Heart characteristic of hypertension, with coronary sclerosis and mural thrombosis of left ventricle; chronic passive congestion of liver; normal gastro-intestinal tract; occlusion of origin of superior mesenteric artery by embolus and thrombus	Death probably from cardiac failure before intestinal infarction could supervene.
5	78 M	Patient under treatment in hospital for cardiac decompensation; was improving gradually when he suffered sudden severe abdominal pain with vomiting and high pulse rate; was in shock 24 hours later when he died	Valvular thrombus of left ventricle; generalized peritonitis; 1,000 c.cm. bloody ascitic fluid; infarction of jejunum, ileum, and right half of colon, and this portion of bowel contained black bloody material, superior mesenteric artery occluded at origin by large thrombus extending into main branches	Origin of embolus from cardiac valvular thrombus.
6	65 M	Patient in hospital for fourth attack cardiac decompensation; right leg amputated for arteriosclerotic gangrene and 3 days later suffered severe spasmodic abdominal pain, vomiting, and progressive abdominal distention; signs of general peritonitis developed; patient died in 48 hours	Practically all of small intestine infarcted due to occlusion of mesenteric artery and its branches by thrombi superimposed on marked arteriosclerotic thickening of the vessels	Mesenteric arteriosclerosis and thrombosis.
7	69 F	For 2 days patient had had vomiting, severe pain in upper right quadrant of abdomen, progressive distention and signs of generalized peritonitis; death 7 days after medical attention given; similar attacks had occurred for 2 years; cholecystectomy performed 1½ years before admission	Infarction of jejunum, ileum, and proximal part of cæcum; occlusion of superior mesenteric artery by arteriosclerotic thickening and superimposed thrombosis	Lesions similar to Case 6 history indicates previous intermittent mesenteric claudication.
8	31 F	Nine days after removal of large infected dermoid cyst of ovary sudden severe abdominal pain developed with vomiting and rise in pulse rate; death occurred 17 days after operation with signs of general peritonitis	General peritonitis; about 2 liters brownish pus in peritoneal cavity; infarction of 1 meter of jejunum with many perforations; superior mesenteric artery filled by thrombus starting 2 cm. from origin of artery; septic infarcts in left kidney and spleen	Generalized sepsis with probable arteritis.
9	27 M	Patient found unconscious in street passing bloody fæcal material; died on way to hospital	Infarction of entire ileum and larger part of jejunum; occluding thrombus filled all of upper part of superior mesenteric artery	Sepsis of unknown origin.
10	62 M	Patient had severe abdominal pain, vomiting, and bloody diarrhœa for 3 days; death occurred shortly after admission to hospital	Infarction of 15 cm. of distal part of jejunum; occlusion of superior mesenteric artery beginning 1 cm. distal to its origin and extending to main branches; infiltration of mesenteric arteries with lymphocytes; 200 c.cm. bloody ascitic fluid.	Etiology similar to Cases 8 and 9.
11	33 F	Patient's blood pressure around 200 systolic for 3 years; death occurred suddenly without abdominal symptoms while patient was sitting up in bed	Entire gastro-intestinal tract normal in appearance; superior mesenteric artery occluded at origin by thrombus; 3 liters of blood in peritoneal cavity; death from large cerebral hæmorrhage	Indeterminate etiology; death before intestinal infarction took place.
12	75 M	Onset of sudden severe abdominal pain, distention and vomiting; patient rapidly went into shock; auricular fibrillation occurred	Infarction of entire ileum; thrombosis and sclerosis of superior mesenteric artery and its branches; 300 c.cm. of turbid fluid in peritoneal cavity	Possibly auricular thrombus.
13	46 M	Patient suffered severe abdominal pain, pulse was feeble, and gradually increasing shock ended in death in 2 days; had been under treatment for about a year for pyelonephritis and nephrolithiasis	General peritonitis; 400 c.cm. bloody fluid in peritoneal cavity; infarction of entire ileum; thrombosis of all mesenteric vessels, and occlusion of superior mesenteric arteries at origin by thrombus; right pyonephrosis with renal abscesses	Severe sepsis originating from pyonephrosis.
14	71 M	Onset with vomiting and passage of several watery stools; severe abdominal pain most marked in lower left quadrant for 4 days; death soon after admission to hospital	Infarction of entire ileum; superior mesenteric artery obliterated at origin by firm clot extending into some of the smaller branches	Mesenteric arteries closed by thrombus.

TABLE II.—Continued

Case	Age Years, Sex	Clinical history and observation	Observations at necropsy	Comment
15	60 M	Epigastric pain, abdominal distention, and vomiting for several days; death 6 days after onset with signs and symptoms of general peritonitis	Gastro-intestinal tract normal except for retrocæcal, subacutely inflamed appendix; superior mesenteric and portal veins distended and occluded by thrombi; 1,500 c.cm. grayish-yellow fluid in peritoneal cavity	Source in appendix.
16	51 M	Onset with sudden pain in lower portion of abdomen with vomiting and signs of shock; death soon after admission to hospital	Infarction of entire jejunum and ileum; superior mesenteric vein and all its tributaries plugged by thrombi; 100 c.cm. of bloody fluid in peritoneum; large abscess in pelvis evidently of appendiceal origin	Source in abscess of appendiceal origin.
17	30 M	Severe abdominal pain and distention for 4 days; constipation for 3 days preceded by diarrhœa; death with signs of general peritonitis	General peritonitis; infarction of entire ileum; gangrenous appendix; thrombosis of vessels of mesentery corresponding to infarcted region	Source in gangrenous appendix.
18	47 M	Severe pain in right lower quadrant of abdomen for 1 week; appendectomy twelfth day after onset at which appendix found acutely inflamed and abscess in meso-appendix discovered; postoperative course stormy with much abdominal pain; death on twenty-eighth day after operation with symptoms of peritonitis	Generalized peritonitis; 1,500 c.cm. pus in abdominal cavity; infarction of 30 cm. of ileum and veins in corresponding region occluded by thrombi; multiple small hepatic abscesses	Source in abscess of meso-appendix and appendicitis, with extension into liver and formation of abscesses there.
19	76 F	For several days tenderness in right lower abdominal quadrant with vomiting, diarrhœa, and absolute obstruction; then signs of increasing peritonitis and death nine days after onset	General peritonitis; infarction of 20 cm. of ileum; appendix retrocecal, gangrenous, and perforated in several places, with a large pocket of pus in its neighborhood	Source, acute appendicitis.
20	60 F	Constipation for one week; nausea, vomiting, and diffuse abdominal pain for 2 days; admitted to hospital in shock; left arm cyanotic and cold and left brachial artery palpable as thick cord	Distal 120 cm. of ileum infarcted; acute suppurative enteritis in corresponding regions; right pulmonary artery, superior mesenteric vein, portal vein, and left brachial artery occluded by thrombi; 300 c.cm. of free blood in peritoneal cavity	Probable source, acute suppurative enteritis.
21	33 M	No clinical data available	Infarction of entire jejunum; superior mesenteric vein occluded by thrombus extending into portal vein; marked fatty metamorphosis of entire liver; 500 c.cm. dark, blood-stained fluid in peritoneal cavity	Hepatic disease with stagnation in portal system.
22	61 M	Patient had had disease of gall bladder for a number of years; the liver was torn in attempting to remove the gall bladder; death occurred on seventh day after operation with symptoms of peritonitis	Infarction of a loop of ileum; occlusion of superior mesenteric vein by thrombus; cholecystitis and cholelithiasis; infected lacerated hepatic substance near gall bladder	The infected hepatic wound resulted in thrombosis of one of the tributaries of the portal vein.
23	25 M	Chills, fever, vomiting, abdominal pain, and diarrhœa lasted 1 week; the liver became enlarged and jaundice appeared; death occurred 18 days after onset with symptoms of peritonitis	Purulent thrombosis of the portal and superior mesenteric vein; multiple hepatic abscesses; 300 c.cm. greenish fluid in abdominal cavity; escherichia coli recovered from the pus	Hepatic abscesses with sepsis in portal system resulted in thrombosis.
24	30 M	For several days severe generalized abdominal pain was present, most marked in right lower quadrant and distention and vomiting occurred; appendectomy was done and patient died in shock 5 days after operation	Infarction of entire jejunum and ileum, and proximal part of colon; corresponding small veins occluded by thrombi but main branches free of clot; no peritonitis; liver enlarged, Laennec's cirrhosis (2650 gm.)	Source in inflammation in tributary of portal system superimposed on stasis due to hepatic cirrhosis.
25	30 M	Patient suffered from constipation and hæmatemesis for 4 days; abdomen was distended and tender and a smooth mass was palpable just below the left costal margin; 75 cm. of gangrenous intestine was resected; the patient died 48 hours after operation	Infarction of 125 cm. of the middle portion of the ileum; occlusion of corresponding veins by thrombi; thrombosis of splenic and portal veins; small amount of bloody fluid in peritoneal cavity; spleen enlarged and adherent to surrounding structures	Source possibly thrombosis of a splenic vein with splenomegaly and secondary thrombosis of the portal and mesenteric veins.
26	64 F	Onset with sudden abdominal distention, high temperature, and rapid pulse; 3 years prior to admission hysterectomy was done for uterine carcinoma; the patient was very emaciated and weak and died within 12 hours from the onset; at the time of death there was roentgenologic evidence of metastasis to the pelvic bones	Infarction of ileum and cæcum; occlusion of corresponding veins with thrombi; many infected decubitus ulcers	Possible cause, mesenteric phlebitis.
27	42 F	On the fifth day after normal delivery the patient's abdomen became markedly distended and tender and she vomited frequently; a mass was palpable in right lower abdominal quadrant; laparotomy only was done; patient died on the seventh day after delivery	Infarction of ileum near ileocæcal valve and of cæcum and descending colon; thrombosis of corresponding veins	Source was inflammatory process introduced at labor.
28	65 F	Onset was with severe diarrhœa and abdominal pain; later there was fever and elevation of pulse rate; an indefinite tumor was palpable in the left side of the abdomen; patient died in 7 days	Proximal 100 cm. of ileum infarcted; veins in corresponding regions filled with clot; 500 c.cm. of bloody fluid in peritoneal cavity	Evidence of an infectious process not noted.

TABLE II.—Continued

Case	Age Years, Sex	Clinical history and observation	Observations at necropsy	Comment
29	32 M	After 2 months of abdominal cramps, epigastric pain, chills, and fever, severe abdominal pain, hæmatemesis and distention suddenly occurred; death resulted in 4 days	Entire gastro-intestinal tract normal; there was very old thrombosis of the splenic vein; the inferior mesenteric vein and the veins over the stomach were recently thrombosed; the superior mesenteric and portal veins were free of clot	Collateral circulation no doubt was established but was not demonstrable.
30	74 M	Severe abdominal pain, vomiting, and complete obstruction were present for 2 days; marked distention supervened, the patient went into shock, and death occurred 3 days after onset	Infarction of the distal two-thirds of the small bowel, the cæcum, and the proximal part of the ascending colon; thrombosis of the corresponding vessels; general peritonitis; myocardial scar of the left ventricle; healed infarct of one kidney	Source probably embolism of the mesenteric artery of cardiac origin.
31	67 M	Laparotomy done for acute intestinal obstruction; an omental band was released; immediately after operation vomiting and signs of peritonitis appeared; death occurred 6 days after operation	Infarction of 50 cm. of ileum, about 125 cm. from the ileocæcal valve; thrombosis of all corresponding mesenteric vessels; general peritonitis; 500 c.cm. of bloody fluid in abdominal cavity	Thrombosis and infarction followed intestinal obstruction.
32	64 M	The history was of inguinal hernia incarcerated for 4 days, of exploration and replacement of apparently viable bowel; symptoms of intestinal obstruction persisted and the patient died 5 days after operation	Infarction of a loop of ileum 60 cm. long lying 15 cm. from the ileocæcal valve; corresponding mesenteric vessels occluded by thrombi	Etiology similar to Case 31.
33	42 F	Sudden onset of severe, steady, generalized abdominal pain, vomiting, and marked prostration; death occurred 36 hours after onset	Infarction of 95 cm. of ileum lying 10 cm. from ileocæcal valve; thrombosis of corresponding vessels; 1,500 c.cm. of bloody ascitic fluid	No cause of thrombosis demonstrable.
34	22 M	Onset with sudden abdominal pain, vomiting, and rise in temperature; 3 months previously patient had undergone colostomy for inoperable carcinoma of rectum and had had some symptoms of obstruction; death occurred 4 days after onset of acute attack	Infarction lower part of jejunum; peritoneal carcinomatosis; infiltration of mesentery and its vessels by malignant tissue	Thrombosis due to invasion of vascular wall by malignant growth.
35	38 F	Onset with sudden nausea, vomiting, extreme prostration followed by several watery stools and severe general abdominal pain; for 6 weeks the patient had suffered from cardiac decompensation due to mitral stenosis and auricular fibrillation; death occurred 48 hours after onset of acute symptoms	Infarction of jejunum and ileum; thrombosis of entire mesenteric artery and its main branches; mesenteric veins near intestinal border occluded by thrombi; generalized peritonitis	Embolism resulting from auricular thrombosis; venous thrombosis secondary to intestinal infarction.
36	64 M	Patient had severe abdominal pain, distention, and vomiting for 3 days; he was moribund on admission to hospital and died soon afterward	Infarction of distal 15 cm. of ileum, appendix, and proximal 20 cm. of cæcum and ascending colon; thrombosis of mesenteric veins in this region; arteries free of clot except the superior mesenteric at its origin which was occluded by thickened sclerotic walls and a thrombus; generalized peritonitis with 1,000 c.cm. of pus in the peritoneal cavity; abscess of spleen	Thrombus probably formed on basis of old sclerosis of mesenteric arteries; venous thrombosis following intestinal infarction.

of the corresponding artery. Experimentally, lesions varying from extensive intestinal infarction to slight ulceration of the mucosa may be produced. The pathological changes noted in the 36 cases are given in Table III.

An infarcted coil of intestine characteristically contains a fluid or semi-solid material varying in its content of blood; it may be almost pure blood. Gangrene and peritonitis is the almost inevitable end-result in the cases in which resection is not performed. Bloody peritoneal fluid, when present, is almost a pathognomonic sign of gangrene. The peritoneal fluid in the cases of this series was found to be as is recorded in Table IV.

Intestinal perforation is uncommon in this condition. It was found in only 1 of the 36 cases. However, peritonitis, either localized or generalized, is commonly found (Table V).

The symptoms of this disease may be either acute and fulminating, or of gradual and phlegmatic onset. At best the symptoms are practically the same as those of any intra-abdominal catastrophe, and the diagnosis between arterial and venous occlusion is usually impossible.

The postulates of Kussmaul and Gerhardt, regarding conditions which should be present to justify a diagnosis of this disease, may well be quoted here, for they agree closely with the phenomena found in this series: (1) a source of an embolism; (2) melena, not to be accounted for by a primary intestinal lesion; (3) rapid and excessive fall of temperature; (4)

TABLE III.—SITUATION OF INFARCTION

	Arterial changes, cases	Venous changes, cases	Arterial and venous changes, cases
Infarction of the jejunum only	1	1	0
Infarction of the ileum only	4	7	3
Infarction of the jejunum and ileum	6	2	2
Infarction of the ileum and colon	1	3	1
No intestinal changes	2	3	0

TABLE IV.—PERITONEAL CONTENT

	Bloody fluid, cases	Clear or turbid fluid, cases	No excess fluid, cases	Fluid not stated, cases
Arterial occlusion	8	2	2	2
Venous occlusion	8	2	3	3
Combined arterial and venous occlusion	4	0	1	1
Total	20	4	6	6
Per cent	55	11	17	17

TABLE V.—INCIDENCE OF PERITONITIS

	Localized, cases	Generalized, cases	Stated to be absent, cases
Arterial occlusion	7	3	3
Venous occlusion	1	5	6
Combined occlusion	0	3	0
Total	8	11	9
Per cent	22	31	25

TABLE VI.—DURATION OF SYMPTOMS

	Seven days or less		Eight days or more	
	Cases	Per cent	Cases	Per cent
Arterial obstruction	10	91	1	9
Venous obstruction	8	57	6	43
Combined obstruction	6	100	0	0

severe, colicky abdominal pain; (5) later, distention of the abdomen with tympanites and shifting dulness; and (6) embolic phenomena elsewhere in the body.

The tendency of arterial and of combined arterial and venous occlusion is to run a more rapid and fulminating course than that in cases of venous occlusion. This is illustrated in the 31 cases of this series in which the duration was stated (Table VI). In addition, venous thrombosis is more likely to be a condition of more vague symptomology and interwoven with signs of preceding disease.

In the differential diagnosis, one must consider other forms of mechanical obstruction, such as volvulus, intussusception, stenosing malignant lesions of the colon, and also acute pancreatitis or ruptured abdominal viscus. The prognosis in this disease is practically 100 per cent fatality without surgical intervention, and even with surgical intervention only occasional cures may be expected.

SUMMARY

A review of 36 cases of mesenteric vascular occlusion in which necropsy was performed is presented. The patients were aged 22 to 78 years, the average being 52.2 years. In 26 cases the patients were men and in 10 cases, women. The most common cause of arterial embolism was mural cardiac thrombi. The most common causes of arterial thrombosis were arteritis, and arteriosclerosis of the mesenteric artery. Venous mesenteric occlusion most often resulted from a septic process either in the gastro-intestinal tract or the pelvis and was of the ascending type. Less often, it was a descending process caused by thrombosis in the portal vein. It followed hepatic disease in 25 per cent of cases. The vascular occlusion affected the arteries in 14 cases, the veins in 16, and both veins and arteries in 6. In all cases of arterial occlusion and in all but one of the cases of venous occlusion, the superior mesenteric vessels were involved. A definite source of the vascular occlusion either was unknown or was problematic in 8 of the 36 cases. Hæmorrhagic infarction resulted in 31 of the 36 cases. When intestinal infarction took place, it was generally manifested by symptoms of intestinal obstruction which were indistinguishable from those of other types of obstruction. Typically, it occurred in an elderly person, starting with extremely severe, colicky abdominal pain, nausea, vomiting, and diarrhœa. The vomitus and the diarrhœal stool were often mixed with blood. Occasionally, complete retention of fæces was noted. Soon the pain became steady, the shock more severe, the abdomen distended and tympanitic, and the temperature and pulse, which at first were likely to be subnormal, became progressively elevated. Later, signs of general peritonitis developed and death took place. In a few cases an abdominal tumor could be palpated. Arterial occlusion, and combined arterial and venous occlusion, presented symptoms which were usually more acute and fulminating than those of venous closure. The symptoms produced

by closure of the main trunk were indistinguishable from those produced by obstruction of the branches. The course of the disease is short and may be less than 48 hours. In at least 53 per cent of the cases, definite peritonitis was present, and in 55 per cent bloody ascites was noted.

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AUTO-INTOXICATION AND SHOCK

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In recent years the problems of the surgeon have become more varied and quite complex. Previously the surgeon considered that he had discharged his obligations to the patient when he had removed the pathological process, controlled hæmorrhage, and avoided sepsis.

The thinking surgeon of today realizes that the outcome of an operation may depend as much upon the condition of the tissue left in the body as upon the removal of the pathological tissue. The history of surgery shows a gradual development of respect for the tissue surrounding the operative field. The rapid operation generally necessitating rough handling of tissue and the use of wide jawed clamps, has given way to a more delicate technique and the use of the narrow jawed clamp. Some operators have even gone so far as to handle tissue with ligatures, using clamps only when absolutely necessary.

The experiences of the war did much to reveal the dangers from absorbing extracts of *freshly crushed tissue* and extracts from *autolyzed tissue*. It soon became evident that a wound freed of dead and dying tissue gave the patient a much better chance for recovery.

DEFINITION OF TERMS

The term auto-intoxication is usually used to denote a toxic condition, self-imposed, which develops through the absorption of toxic material from the gastro-intestinal tract. In the following discussion the term is used to denote a toxic condition, self-imposed, which develops through absorption of extracts of body tissues. Such auto-intoxication is presented under the two divisions; (1) that produced by extracts of fresh tissue, and (2) that produced by the extracts of autolyzed tissue.

THE ACTION OF FRESH TISSUE EXTRACTS

In 1922, Cannon published his splendid report on "Evidence of a Toxic Factor in Wound Shock." In the study of "wound shock" Cannon described his experiment as follows: "In order to bring about, in lower animals, a traumatization similar to that giving rise to shock in man, the thigh muscles

in the anæsthetized cat, while being supported by an iron block, were repeatedly struck with a blunt wedge-shaped hammer, or they were crushed by compression. The trauma usually failed to break the skin, so that infection from without was impossible." After about 20 minutes the blood pressure of such animals began to fall, and after about 1 hour it had usually fallen to shock level. That the toxic material is carried in the circulation was demonstrated by Cannon in the following manner: the blood vessels of the leg were ligated before the muscles were crushed, and the ligatures were left in place for 33 minutes after the trauma, during which there was no fall in blood pressure. However, as soon as the blood flow was re-established the pressure promptly fell to a low level.

In previous reports (7) we have called attention to the changes produced in blood pressure by the intravenous administration of saline extracts of fresh tissue. Figure 1 shows a record of blood pressure and respiration obtained from a dog. The changes in blood pressure level are due to the intravenous administration of a saline extract of fresh liver. The extract was produced by grinding fresh dog liver with an equal amount of physiological salt solution, the ground mass was then filtered and the filtrate used while fresh. Administration of 0.5 cubic centimeters shows a definite fall in blood pressure while the injection of 10 cubic centimeters gave a marked lowering of blood pressure. It will be noted that the normal blood pressure was 60 millimeters above the base line and the lowered blood pressure recorded less than 30 millimeters above the base line. With the exception of suprarenal and pituitary extracts all fresh tissue extracts possess this property of lowering blood pressure.

Mason has previously (6) called attention to the extreme potency of fresh tissue extract in the production of intravascular coagulation (thrombosis and embolism). If three drops of fresh lung tissue extract be injected into the circulation of a rabbit, it will produce coagulation of all the intravascular blood in about 20 seconds. All the fresh tissue extracts share this potency, but the degree of potency varies with the tissue used. The actual amount of fresh tissue extract necessary to produce death, through thrombosis, is very small; such extracts contain 3.65 per cent solids, 0.9 per cent of which is the salt added. The actual solids in the crude preparations is not more than 2.75 per cent. Since only 3 drops is necessary to produce complete thrombosis of the entire vascular system, the actual amount of crude material used is only .0055 grams.

ACTION OF EXTRACT OF AUTOLYZED TISSUE

If a small piece of liver is deprived of its circulation and is left in the abdomen, the animal will die, death usually occurring in 15 to 18 hours (7, 8, 9). We have recently studied 16 more animals in an attempt to determine the nature and action of the toxic material generated in liver tissue deprived of its circulation. If the partially autolyzed liver is removed at the death of the animal and ground with salt solution, it yields an extract which possesses properties different from salt extract of fresh tissue. Figure 2 shows a record of blood pressure and respiration obtained from a dog. It will be observed that the amount of extract injected was the same as used in Figure 1; however, the blood pressure response is quite different. There is an initial fall of blood pressure in both records, but with sublethal doses of the autolyzed tissue extract the blood pressure always returns to a higher level than before the injection. In previously published work (8), we have shown that the heart becomes irregular with small doses, and we have also determined the fatal dose to be about 7 to 8 cubic centimeters. Figure 3 is presented to illustrate the effect of injecting 10 cubic centimeters of the extract of autolyzed liver. It will be noted that the dog died almost instantly. The death produced by the administration of extract of autolyzed liver occurs after destruction of the central nervous system and paralysis of the vagal endings.

USE OF TANNIC ACID

While studying the toxic action of autolyzed tissue, our attention was focused on the toxic condition accompanying burns. We early conceived the idea that absorption of the products of decomposing dead and dying

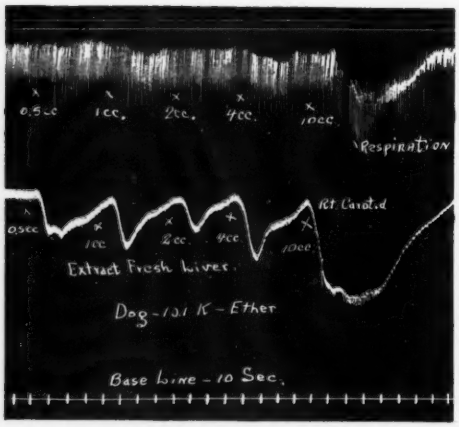

Fig. 1.

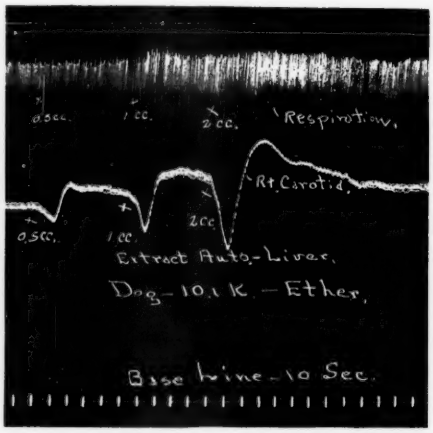

Fig. 2.

tissue contributed largely to the cause of death from burns. Davidson, acting on the suggestion of Mason, instituted the use of tannic acid as a treatment for burns, the object being to precipitate the products of decomposition brought about by the destructive action of burns. The splendid work of Davidson, which has been so completely confirmed by many subsequent workers, has proved the value of such a method of treatment.

Assuming that the autolysis of skin and the autolysis of liver liberated the same toxic substance, we have studied the toxic action of the autolyzed liver treated with tannic acid. Figure 4 shows the effect on blood pressure and respiration produced by the filtrate of the tannic-acid-treated autolyzed liver extract. We used 4 per cent tannic acid solution in order that our resultant mixture would have a concentration of not greater than 2 per cent tannic acid, which is the concentration of tannic acid used in burns. The filtrate was water clear and doubtless contained but little tannic acid.

It will be noted that the filtrate was still very potent, causing a thready, irregular pulse followed by a marked rise in blood pressure. It is evident that tannic acid removed little, if any, of the toxic element. The action of tannic acid administered intravenously is not similar to the results obtained in Figure 4, but varies considerably with the amount injected. Figure 5 is presented to show the effect of administering doses of tannic acid, large enough to kill.

DEDUCTIONS

During the past year Blalock has repeated the experiments of Cannon and Bayliss "in order to try to determine whether the low blood pressure produced by trauma to one of the extremities is due to the formation of some substance which exerts general bodily effect or whether it is due simply to hæmorrhage locally."

His summary contains the following: "The blood pressure could not be reduced to a shock level by trauma to one of the posterior extremities without causing the loss of a sufficient part of the blood volume into the traumatized area to account for the decline in the pressure." Blalock dismissed the rôle of tissue extracts by saying: "A great deal of work has been performed to determine the effects on the blood pressure of the injection of extracts of various tissues, of the products of autolysis of crushed muscle and of many other substances. Most of these substances caused a decline in the blood pressure. No evidence for the action of these products was found in the present experiments. Many of the substances which were studied are supposed to be fairly closely related to histamine. Goodpasture found that a fresh extract of the pancreas produced changes in the gall bladder similar to those observed by Bradburn and

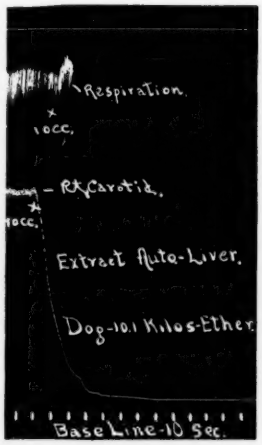

Fig. 3.

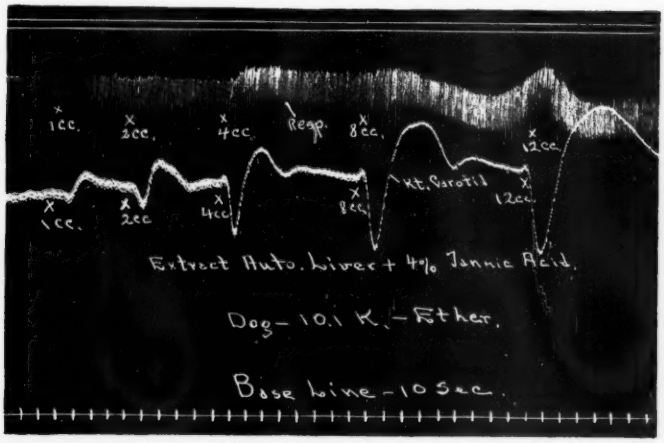

Fig. 4.

Blalock after the injection of histamine. Trauma to the extremities did not produce any alteration in the gall bladder."

The observations of Blalock have been recently confirmed by Parsons and Phemister. They stated: "Traumatism of a limb of a dog producing fall in blood pressure is accompanied by a corresponding increase in limb volume and anæmia which are due very largely to hæmorrhage into the damaged tissues." In these experiments it could not be demonstrated that a toxic substance liberated from damaged or asphyxiated tissues or extravasated blood of the limb was absorbed and produced a sustained fall in the general blood pressure.

It is difficult to reconcile our findings with those just presented. We suggest that in the studies involving the use of crushed muscle, the conclusions were formulated due to one of the three following reasons: (1) the tissue extract from the fresh tissue failed to reach the general circulation; (2) the tissue was not allowed to undergo autolysis; or, (3) muscle tissue does not yield as toxic a substance as does skin or liver tissue. The figures in Table I represent the changes in weight of liver tissue left free in the abdomen until it caused death (15 to 18 hours). The first column represents the amount of liver sectioned at operation; the second column the amount of liver at the death of the animal; and the third column the loss in weight. It will be noted that a loss in weight of as little as 10.5 grams of liver substance caused death; probably only a small fraction of this was absorbed by the animal. Therefore, it is evident that it requires

TABLE I.—CHANGES OF WEIGHT IN LIVER TISSUE LEFT FREE IN ABDOMEN

Fresh liver, grams	Autolyzed liver, grams	Difference, grams
28.5	15	13.5
46.6	35	11.6
34	18	16
50.5	28	22.5
61	43.5	17.5
36.5	26	10.5
65.5	45.3	20.2
84	61	23

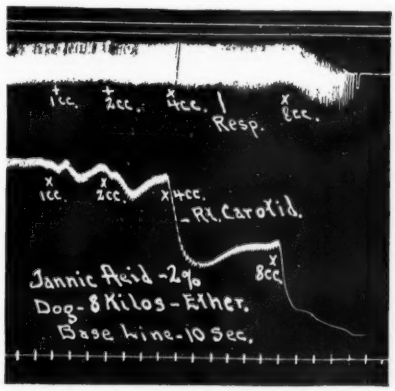

Fig. 5.

only a small amount of some tissues to cause death. Also, the decreased mortality rate with the use of tannic acid in treating burns strongly suggests that its value lies in the precipitation, in insoluble form, of decomposed tissue.

Andrews, Thomas, and Schlegel, discussing the experiments of Mason et al, done in 1924, wrote the following: "These experiments have been criticized on the assumption that this procedure killed the dogs by producing peritonitis, but we have repeated them, inserting the bits of liver into the chest and into the axilla and have had the same results." Very recently Ellis and Dragstedt have reopened the subject and have concluded that death accompanying free liver tissue in the abdomen is due to an anaerobic bacillus. From the experimental data presented, we do not think that these authors have sufficient evidence on which to base their claim. They killed their animals at the end of 15 to 38 days and demonstrated the presence of the organism which they claim causes the death of our animals in 15 to 18 hours. They further showed that fetal liver, both sterile and infiltrated with the anaerobic organism, failed to kill the dogs.

The marked rise in blood pressure following sublethal doses of autolyzed liver extract suggests a possible relation of foci of infection and hypertension. Possibly foci of infection liberate a toxic substance which elevates blood pressure.

CONCLUSIONS

1. Fresh tissue extract administered intravenously lowers blood pressure sufficiently probably to endanger patients who are in a critical condition.

2. Fresh tissue extract is a very potent factor in producing intravascular coagulation.

3. Sublethal doses of autolyzed liver tissue extract causes marked circulatory disturbances, the lethal dose being 7 to 8 cubic centimeters for the dog.

4. Treatment of autolyzed liver tissue extract with tannic acid does not precipitate the toxic fraction.

5. The marked rise in blood pressure following sublethal doses of autolyzed tissue suggests the possibility that foci of infection may liberate a toxic substance which elevates the blood pressure.

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CLINICAL SURGERY

FROM THE SURGICAL CLINIC, UNIVERSITY OF LYON

THE KEHR SUBSEROUS OPERATION

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Professor of the Surgical Clinic of the University of Lyon

THE Kehr subserous operation applies a principle of surgical technique essential to complete any abdominal or intraperitoneal operative procedure, that is, the peritonization of the bleeding surfaces and the shutting off of the field of operation with peritoneum. It is true peritonization of the pelvis, an indispensable final step in hysterectomy, is possible but is it possible to peritonize the lower surface of the liver after a cholecystectomy and the opening of the bile duct, and at the same time to leave a passage for drainage of the hepatic duct? Since 1908 we have shown that this step can be accomplished in about half the cases.

Our modification makes it possible to abandon the Kehr subhepatic tampon. The Kehr tampon is an essential feature of the Kehr method, the object of which is to create a subhepatic barrier by means of inflammatory adhesions which are formed at the expense of the neighboring viscera, thus allowing the subhepatic drain to pass out. The Kehr method has all the immediate and late disadvantages of a Mikulicz operation; all surgeons know its defects; and for this reason they will not be repeated here.

In our modification we use a simple, continuous serous tunnel to carry out hepatic drainage. A few days after the drain is removed the biliary fistula closes by adhesions formed between the two walls of the serohepatic tunnel.

TECHNIQUE

The operation is performed in 3 stages: (1) incision of the wall and liberation of the gall bladder; (2) subserous dissection of the gall bladder and the cystic duct, incision of the bile ducts, exploration and removal of calculi from the chief bile duct, insertion of hepatic drainage, retrograde cholecystectomy; and (3) the making of a serohepatic tunnel around the Kehr drain, the fixation of the lips of this serous tunnel to the parietal peritoneum, and suture of the wall.

In the description of each of these stages we shall mention only the details which differ from those in the classical operation of Kehr.

First stage—incision of the wall and liberation of the gall bladder. Any of the classical incisions for opening the abdomen may be used; we ordinarily use the Kehr-Hartmann type of incision. In this type of incision two cuts are made—one vertical and the other transverse—thus making it possible when completing the operation to choose the most favorable point at which to make the external opening for the serohepatic tunnel through which the Kehr drain comes out.

The vertical incision is made at the external border of the rectus; it is an exploratory incision passing into the abdomen and making possible the confirmation of the diagnosis. If it is found that the Kehr operation is necessary, a transverse incision of the rectus is quickly made with scissors between two fingers introduced into the abdomen. This incision gives access to the subhepatic region.

The gall bladder is liberated and three large compresses are inserted: an internal, a median, and an infero-external one. An ordinary retractor is used. The liver is exposed.

Second stage—subserous dissection of the gall bladder, the cystic duct, and the junction with the common duct; incision, step by step, of the bile ducts; exploration; removal of calculi from the chief bile duct; establishment of hepatic drainage; and retrograde cholecystectomy.

The bottom of the gall bladder is grasped by the assistant with his fingers or with a tenaculum and the lower surface is brought up for incision. If, because of the presence of much liquid the gall bladder is under too great tension or the walls are too thin, it may be advantageous to remove some of the liquid by puncture. However, the following chief step of the operation can be performed better on a gall bladder under moderate tension than on a flabby one.

Fig. 1. Racket incision cutting two flaps of peritoneum. Subserous dissection of the gall bladder, then of the cystic duct, and finally of the common duct.

Fig. 2. The gall bladder is extirpated and the operation on the common duct is performed.

A semicircular incision is made in the serous covering of the lower part of the gall bladder at the junction of the anterior third with the posterior two-thirds of the gall bladder. The proper plane of cleavage is found by making small repeated incisions. The serosa is detached with blunt curved scissors. As soon as the peritoneal flap is well circumscribed, an anteroposterior longitudinal incision is carried to the semicircular transverse incision, and is prolonged to the cystic duct. The incision takes the form of a racket, the loop the part surrounding the lower semicircumference of the gall bladder and the handle the part prolonged to the axis of the cystic duct.

The two flaps are detached either with blunt curved scissors or simply with small gauze tampons mounted on forceps. Small Chaput forceps serve as guides for the edges of the peritoneal flaps. Denudation is easier and more rapid as the region of the pelvis and cystic duct is approached. Hæmostasis is carried out on some small transverse subserous arteries and veins.

The gall bladder which has been freed of its serous covering is carefully placed on compresses and the liquid is aspirated. A longitudinal incision of the gall bladder is made quickly, and calculi are removed. By means of small blunt curved scissors introduced into it, the cystic duct is slit along its lower surface down to its junction with the common duct. This gradual progress toward the common bile duct is the most prudent method and prevents transverse section of either the hepatic or common duct. The common and hepatic ducts are explored and any calculi are removed as usual. Traction on the lips of the cystic duct with forceps facilitates catheterization and brings the ducts before the surgeon, who incises them one by one.

A Kehr T drain, or two drains,[1] one in the hepatic the other in the common duct, establishes drainage of the hepatic duct. The drain is fixed with a small catgut No. ∞ suture to the walls at the junction of the two ducts (Fig. 1).

The gall bladder is now quickly removed by retrograde manipulation after the cystic duct is sectioned. The cystic artery is cut and carefully ligated (Fig. 2).

Variation. When the liquid withdrawn from the gall bladder appears to be virulent and very septic, it is well to section the cystic duct between two ligatures and to perform the cholecystectomy before approaching the junction and the common duct step by step through the cystic duct.

Third stage—making the serohepatic tunnel. Suture of the wall.

The Kehr drain or the two drains from the hepatic and the common ducts are kept buried in

[1]We often prefer to replace the Kehr drain with two separate drains

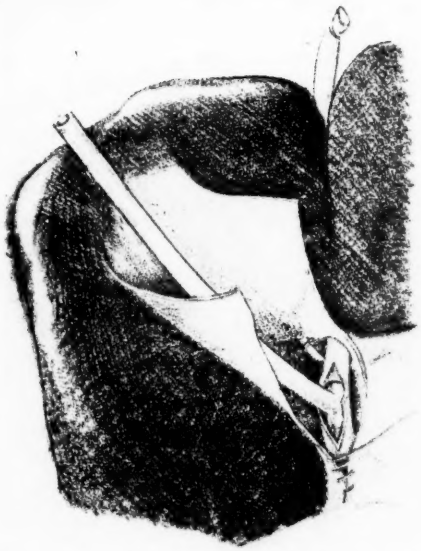

Fig. 3. Drainage of the hepatic with a T drain. Suture of the peritoneal flaps over the drain, forming a serohepatic tunnel.

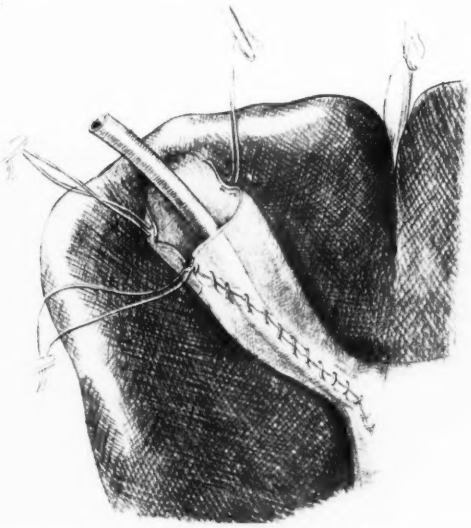

Fig. 4. The suture, bringing the lips of the gall-bladder peritoneum together forms a continuous serous tunnel from the common duct to the wall.

the cystic fossa. A fine catgut suture brings the two peritoneal flaps together in the midline to form a serohepatic tunnel which has an exit at the surface (Fig. 3). This suture begins in the deep tissues at the junction of the ducts and carefully closes the end of the handle of the racket of the primary peritoneal incision beneath the drains. A small needle is used and the suture points are made close together so as to assure the absolute tightness of the serous tunnel. If the peritoneal flaps are loose a second reinforcing suture may be supplemented.

The suture is finished at the bottom of the tunnel. Three suspension sutures, preferably U-shaped, are passed to the angles of the bottom of the tunnel. They are not tied but their free ends are caught in forceps which are handed to an assistant. The surgeon locates the point on the incision in the wall at which it is easiest to fix the serohepatic tunnel and at the same time to cause as little traction as possible and to prevent the bending of the drain. It only remains now to close the abdominal incision and to fix the serous tunnel to the parietal peritoneum at the point chosen. The incision in the wall is carefully sutured, except for the opening in the peritoneum which is the size of a two franc piece and is left opposite the bottom of the tunnel. The tunnel is kept outside the parietal peritoneum by the three suspension sutures mentioned.

A curved Reverdin needle, carrying the two ends successively of each of the U suspension sutures, is passed through the parietal peritoneum, the transversalis fascia, and the aponeurosis (deep layer of the muscle sheath). The sutures are lightly tied, thus assuring as perfect application as possible of the serous tunnel to the parietal peritoneum (Fig. 5).

The skin is sutured with horsehair. Some gauze compresses are placed on the incision in the wall and fixed with leucoplast which covers them completely so as to form a water-tight dressing for 48 hours, during which time a large ice-bag is kept on the abdomen. With a horsehair suture or with a band of leucoplast, the drain or drains are fixed to the skin at a distance.

RESULTS

The postoperative course is very simple when the conditions are carefully studied during the operation and the proper procedure is determined. The drain is removed between the fifteenth and eighteenth days, depending on the temperature curve and the character of the bile, which is watched every day. Generally by the twenty-fifth day cicatrization is complete and the wall is solidly healed. Only for the first 36 hours does the patient have pain which is located at the site

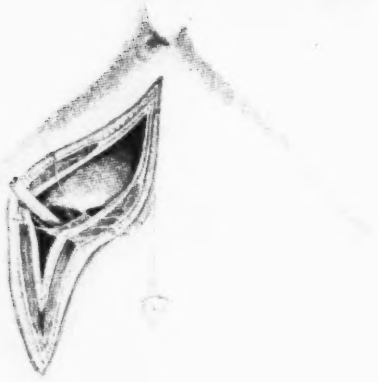

Fig. 5. The bottom of the tunnel is fixed to the parietal peritoneum, leaving a passage for the drain and bringing about complete peritonization of the field of operation.

of fixation of the bed of the gall bladder to the wall. The pain is easily controlled by ice and the use of narcotics, but narcotics should be limited to patients with liver affections. There is not the prolonged pain from peritoneal reaction so often present when the subhepatic tampon is used, also the dreadful trial of removing the tampon, which is always very painful, is avoided. The patient is also protected from the complications—secondary hæmorrhage, postoperative evisceration, intestinal fistula, diffuse peritonitis—which complications are always possible when the tampon has been removed.

There are no late complications, no postoperative eventration, as the wall has been carefully reconstructed, and also no postoperative subhepatic adhesions, as the whole field of operation has been covered with a continuous serous covering.

CONCLUSIONS

This operation, which gives the maximum of both operative safety and simplicity of the postoperative course, cannot unfortunately always be performed and it may be dangerous. According to our personal experience it should be performed only in about half the cases.

It cannot be performed (a) when the gall bladder is very much degenerated, as then it would be impossible to cut peritoneal flaps that are large enough; (b) when the detachment of the peritoneum does not furnish continuous flaps. It is dangerous and should not be performed (a) when suppurations around the gall bladder have been opened in the process of freeing the gall bladder; and (b) when the general condition of the patient is so serious that the operation must be performed as quickly as possible.

The advantages are that it is possible to remove the drain from the common duct early while keeping the drain in the hepatic duct and to collect the bile which comes from the hepatic duct in a sterilized vessel to be reinjected after sterilization in the intestine, through the drain in the common duct. This is a very effective means of combating the rapid emaciation and asthenia following too great a loss of bile after operation.

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FROM THE SURGICAL CLINIC, MEXICAN NATIONAL SCHOOL OF MEDICINE

TREATMENT OF INCISIONS BY THE OPEN METHOD

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OCCASIONALLY it is a good thing to turn aside from the major surgical problems to think a little about some steps in operations which, though they are of relatively little importance, are worthy of study in order to attain the maximum of surgical perfection. Little thought is given to the technique of the last step in a surgical operation—the suture of the skin. Every surgeon has his own routine method, and he does the closure mechanically if he does not turn it over to an assistant. At times poor skin suture causes the surgeon some trouble, necessitates a prolonged stay of the patient in the hospital, and leaves him with a large, ugly, permanent, sometimes painful scar.

This led me to read with great care the method described by Drs. George W. Roberts and Kingsley Roberts, of New York, in the *Annals of Surgery* for June, 1927. After a classification of surgical wounds according to their evolution, to which I will return later, they take up the new point in their article: when the suture of the skin is finished in the manner to be described, a current of hot air is passed over it to dry it, then a sterile compress is placed over it while the patient is being carried to his bed; here the wound is exposed to the air until it is completely dry and then merely covered by the patient's clothes, with no other preparation whatsoever. For the next few days the healing of the wound is simply watched and no medication is used unless some accident occurs. The method deserves its name and is a distinct break from the old custom of covering a wound with gauze and cotton.

What conditions are necessary to bring about healing of a wound by first intention?

First, the skin should be properly disinfected; second, the steps of the operation should be done under aseptic conditions, or at least care should be exercised not to contaminate the lips of the wound; and, finally, the skin should be correctly sutured, that is to say, not only under the most rigid asepsis, but hæmostasis must be complete and the skin edges accurately coapted. If all these conditions are fulfilled it is necessary that the wound be covered only with a thick layer of aseptic gauze or that it be left in contact with the patient's clothes. A thin membrane forms over the suture line of the skin surfaces which protects the process of cicatrization and completely isolates the wound from the external air. This is the fundamental principle of the method and the reason for its success.

The technique which we use to bring about proper cicatrization is briefly as follows:

Except in emergency cases the skin of the patient is sterilized the evening before the operation by washing it with water and sterile soap and shaving the parts where shaving is necessary; the skin is rubbed with 96 per cent alcohol, then with a 0.5:1000 mercury iodide solution, and last with Harrington's solution. The skin is dried with cotton and covered with compresses of sterile gauze held in place with a bandage. This dressing is

Fig. 1. Suture carrying needle at either end.

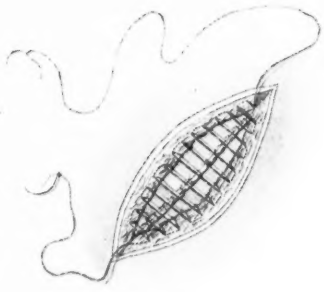

Fig. 2. Medium sized needle laid aside temporarily.

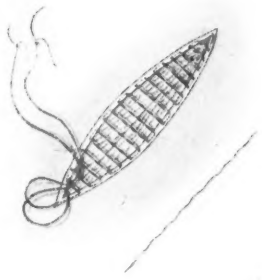

Fig. 3. The wound shows slightly wavy line.

POSTOPERATIVE COURSE OF INCISIONS

Number ..... Room ..... Date .....
Name ..... Subject: Fat, Medium, Thin
Operation .....
Preparation of the skin .....
Operator ..... Assistants .....

Type of incision ..... (cms.)
Suture: Peritoneum .....
Deep aponeurosis .....
Muscle .....
Superficial aponeurosis .....
Fatty cellular tissue .....
Skin .....
Canalization .....
Antisepsis of the skin after closure .....
Did the skin hold? .....
Was there any defect in technique? .....
Was there any reason for the skin not healing by first intention? .....

1st day	6th day	11th day .....
2nd day	7th day	12th day .....
3rd day	8th day	13th day .....
4th day	9th day	14th day .....
5th day	10th day	15th day .....

Abbreviations: P, pus; S, serum; Sa, blood; G, gas; #, without complications; Sep., separation of the skin.

Classification .....

Fig. 4. Record sheet used at Valdes Sanatorium.

taken off the next day, and when the patient is on the table the field is painted with tincture of iodine shortly before operation is started.

A layer of sterilized rubber is placed over the skin which is incised as if it were the first layer, and when the skin has been sectioned the sterilized rubber is fixed to it by clamps, thus protecting the skin from all septic contact.

The technique for the superficial layers was described by Dr. Ignacio Franco, interne of the hospital, in a preliminary communication made to the Eighth National Medical Congress.

When the deep layers have been closed to the superficial aponeurosis, the subcutaneous cellular tissue and the skin are sutured in the following manner: with a suture of twice the usual length threaded into a fine needle at one end and into a medium sized one at the other, the suture is begun by passing the thread into the fatty cellular tissue at one of the angles of the wound and tying it in the middle, so as to leave two threads of approximately the same length with a needle at each end (Fig. 1).

With the medium sized needle, a Cushing suture is run to the opposite end of the wound and this thread and needle are then laid aside temporarily (Fig. 2). When the Cushing suture is finished the fine needle is taken up and after one or two stitches backward in the cellular tissue, which make it possible to begin an intradermal suture at the end of the wound, this suture is continued with the same technique as the other one to the opposite end of the wound. The two sutures, the one in the fatty cellular tissue and the intradermal one, pass beneath the two last stitches of the intradermal one (Fig. 3), are pulled together to bring about perfect coaptation, and the superficial and deep threads are tied, with the ends very short, so they may be hidden beneath the skin suture. The wound shows a slightly wavy line.

The postoperative care is the same as that used by the authors before mentioned: when the suture is finished and the wound is washed with sterile water a current of hot air is passed over it for some minutes; then the region is covered with a sterile compress and the patient is put to bed, after which hot air is passed over the wound again, and it is left in contact with the bed clothes, which are not prepared in any way.

In large abdominal wounds, some strips of adhesive plaster are applied perpendicular to the wound as a support when distention is feared.

A special record sheet shown in Figure 4 is kept, and the wounds are classified in four groups:

Group A. Wounds which during cicatrization have not discharged blood, serum, gas, or pus, except perhaps a slight exudation of blood or serum in the first few hours after operation.

Group B. Wounds which within the first 72 hours have discharged a small amount of blood, serum, or gas, or a small, non-infected clot.

Group C. Wounds which within the first 10 days discharge pus without interfering with the patient's convalescence.

Group D. Wounds in which some complication affects the patient's convalescence, such as extensive infection or spontaneous rupture.

We have selected a group of 110 wounds in which no canalization or other process affected normal cicatrization. The results were as follows: Group A, 93, 78 per cent; Group B, 20, 16 per cent; Group C, 6, 5 per cent; Group D, 0.

Taking into consideration the fact that Group B are wounds in which there was only a slight discharge of blood or serum which did not disturb cicatrization and that on leaving the hospital except for a slight disturbance in healing they were completely cicatrized, like those in Group A, we have a total, in Groups A and B, of 113 successful results in 119 cases, or 94 per cent.

These excellent results have led us to describe this method for the benefit of others.

THE TREATMENT OF MAMMARY CARCINOMA BY MEANS OF REMOVABLE RADIUM NEEDLES[1]

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THE purpose of this communication is to describe an improved method of interstitial radiation which has yielded satisfactory primary regressions in types of inoperable breast carcinomata that have failed to respond to other radiotherapeutic methods. It is not within the scope of this paper to discuss in detail the various stages through which the radiation treatment of mammary carcinoma have passed. The marked limitations of external radiation—X-rays and radium—in the treatment of mammary carcinoma are now fully recognized. Neither will it be attempted to discuss the relative merits of surgery and radiation in the treatment of *operable* mammary carcinoma since the evidence today does not yet permit a decision on this important question. The text of this communication will deal primarily with the treatment of *inoperable* carcinoma of the breast by interstitial radiation.

DIFFICULTIES IN THE RADIATION TREATMENT OF MAMMARY CARCINOMA

Several important difficulties are encountered in the radiation treatment of mammary carcinoma:

1. The presence of carcinoma in areas of the breast that are apparently normal on clinical examination render it imperative to regard the entire organ as invaded by carcinoma when treatment is planned.

2. The presence of disease in the areas of lymphatic drainage when no disease can be detected clinically renders it necessary to assume that these areas too are invaded even when no evidence of disease can be made out by clinical examination. The same underlying principle that ordains the radical operation for a small and apparently localized mammary carcinoma necessitates radical irradiation of the entire field if the latter method is to be employed successfully; with these considerations it is necessary to irradiate the entire breast, the axillary contents, and supraclavicular space without consideration of the size of the primary tumor or the extent of the disease. Thus the problem resolves itself into that of delivering to this wide field a uniform, homogeneous, and adequate dose of radiation if a complete and certain sterilization of this potentially invaded field is to be expected.

3. Were mammary carcinoma sufficiently radiosensitive to permit of the delivery of a lethal dose to the tumor cells by means of external radiation alone, the radiation treatment of mammary carcinoma would be greatly simplified. In small thin breasts, an actual sterilization of the tumor by intense external radiation with radium has been accomplished in a small group of cases. When the breast is large and fat, the geometrical conditions are more unfavorable and the delivery of an intense and uniform dose of radiation by surface application is considerably more difficult.

4. The anatomical relations of the axillary lymphatic glands render it almost impossible to deliver an adequate and uniform dose of radiation to these structures without injuring the skin and

Fig. 1, left. Extensive carcinoma of breast with impending ulceration before treatment. (Case 1.)

Fig. 2. Complete disappearance of lesion seen in Figure 1 (Case 1) following interstitial radiation.

Fig. 3, left. Extensive ulcerated carcinoma of breast before treatment. (Case 2.)

Fig. 4. Complete disappearance of tumor and healing of ulceration (Case 2) after interstitial radiation.

[1]From the New York City Cancer Hospital. This investigation was made possible through the support of the Lucius N. Littauer Fund for Cancer Research, New York University.

Fig. 5. X-ray of chest showing arrangement of radon needles in Case 1.

the important axillary vessels and nerves. The difficulty of efficiently irradiating the axillary lymphatic glands constitutes the most important barrier to the successful treatment of carcinoma by means of radiation.

THE RADIOSENSITIVITY OF MAMMARY CARCINOMA

Carcinomata of the breast exhibit notable variations in radiosensitivity. On the whole it may be said that carcinoma of the breast is moderately resistant to treatment with X-rays and radium. Compared with other glandular carcinomata, their radiosensitivity is approximately the same as that of carcinomata of the rectum, stomach, and body of the uterus. If a large series of carcinomata of the breast be treated with maximum doses of X-rays or radium applied externally, three degrees of response can be observed. A small proportion of the tumors respond so slightly that the change is hardly perceptible by clinical examination. The largest proportion exhibit a moderate diminution in size, and a very small proportion show a marked and sometimes rapid response to external radiation. The rapid and complete disappearance of a mammary carcinoma after external radiation is sometimes observed but is a very rare occurrence. These variations in radiosensitivity of mammary carcinoma are not unusual. Similar variations are noted in carcinomata affecting other organs.

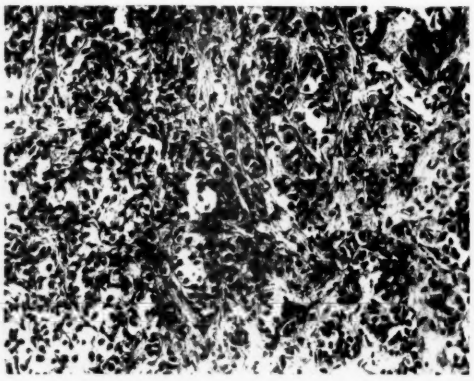

Fig. 6. Photomicrograph of biopsy specimen taken from ulcerated lesion in Case 2. (Fig. 3.) The structure shows infiltrating duct carcinoma.

INTERSTITIAL RADIATION IN THE TREATMENT OF MAMMARY CARCINOMA

Because of the limitations in the effect of external radiation on mammary cancer, it becomes necessary in most instances to resort to interstitial radiation in order to deliver a lethal dose to the tumor cells. Interstitial radiation is most efficacious in small, accessible tumors. It is not difficult, for example, to distribute radium needles around a mammary carcinoma with sufficient accuracy to insure its complete sterilization when the tumor is small and the radiation correctly applied. The uniform distribution of radium needles throughout an entire breast—considering all its dimensions—is almost impossible. The most important obstacle in the way of the successful treatment of mammary carcinoma by radiation is the problem of delivering to the axilla an adequate, uniform, and homogeneous radiation.

From examination of mammary carcinomata that have been removed following interstitial radiation, it is at once obvious that the most important cause of failure is the inaccurate distribution of the radium foci. It is important to realize that unless the distribution of the radium foci is uniform the method is doomed to failure. Theoretically, the distribution of radium foci must reach almost geometric perfection, a goal that is impossible to reach under the given conditions. In specimens of mammary carcinoma that have been treated by interstitial radiation (gold radon seeds) in which the distribution has been faulty, I have found scattered foci of viable tumor cells

lying among areas of completely necrotic tumor tissue. In isolated examples in which the distribution has been uniform the destruction of the primary tumor has been so complete that degenerated remnants of several tumor cells were found only after careful search by numerous sections, and these have constituted the only available evidence of preexisting carcinoma.

It is an interesting fact that minute foci of tumor cells that have not been devitalized by radiation can flourish in an avascular tissue medium consisting of necrotic débris. Histological examination of irradiated tumors often shows groups of well staining hyperchromatic cells growing in dense, hyaline, avascular connective tissue, a condition to which Ewing has applied the term "abortive fibrosis." The importance of these observations is that it is these foci that constitute the elements of recurrence and determine the failures in radiation therapy. They also emphasize the necessity of a uniform radiation. The fundamental question that arises in the treatment of mammary carcinoma by interstitial radiation alone is this: Is it technically possible to distribute a large number of radium needles throughout a carcinomatous breast and axilla with sufficient uniformity and accuracy completely to devitalize and sterilize all the tumor cells and thereby accomplish a cure of the disease in these situations?

One of the earliest attempts to treat mammary cancer by interstitial radiation was carried out in the Memorial Hospital by Drs. Lee (3) and Adair. Long platinum radon needles were inserted through the mammary growth and removed after several hours. Some favorable results were obtained by this method, particularly in tumors of small dimensions. The most important objection to this method is that only the palpable tumor was irradiated and recurrences frequently appeared in outlying parts of the breast which appeared clinically normal but were actually invaded by carcinoma. This method was first supplanted by external radiation and more recently by interstitial radiation with gold radon implants. Interstitial radiation of mammary carcinoma with removable platinum needles was also employed by Kaplan[1] in the Bellevue Hospital as early as 1924. An important investigation of the effect of gold radon implants on mammary carcinoma has been conducted recently by Pack[2] on the service of Dr. Lee at the Memorial Hospital. His extensive histological studies of irradiated breast tumors have yielded valuable information concerning the dose of radiation necessary to devitalize a given unit of tumor tissue.

[1] Kaplan, I. Personal communication.
[2] Pack, G. T. Personal communication.

KEYNES'S METHOD OF INTERSTITIAL RADIATION

The most comprehensive and systematic attempt to treat mammary carcinoma by interstitial radiation was begun by Keynes in 1924, and the results were reported in 1928 and 1930. The underlying principles of Keynes's method consist in distributing a number of radium bearing needles containing small amounts of radium (2 and 3 milligrams of radium element) underneath and around the breast tumor and accessible areas of lymphatic drainage. The total amount of radium necessary in the adequate treatment of a mammary carcinoma varies with the size of the tumor between 60 and 90 milligrams. The radium, in the form of radium sulphate, is contained in platinum needles, each containing 3 milligrams distributed along an active length of 4.8 centimeters. For the supraclavicular and infraclavicular regions and the intercostal spaces a few shorter needles containing 2 milligrams of radium element with an active length of 3.2 centimeters are needed. The filtration is 0.5 millimeter platinum.

The radium needles are inserted so that the carcinoma and a considerable area surrounding it are illuminated by the radiations. Needles are also inserted into the axilla, beneath the pectoralis major, above the clavicle, below the clavicle, and over the first three or four intercostal spaces. The needles are allowed to remain in position for at least 1 week and sometimes for as long as 10 days, if the tumor is a large one. They are then removed under gas and oxygen anæsthesia.

An essentially similar method of radiation of mammary carcinoma is employed by Cade with the exception that the interstitial radiation is followed 1 month later by surface radiation. The latter procedure is accomplished by means of a Columbia paste cast which covers the anterior, posterior, and lateral aspects of the chest and supraclavicular areas. Irradiation is continued for 14 days, the average dose being 35,000 milligram hours, in equal halves for each aspect of the thorax. This phase of the treatment aims at the sterilization of the tumor cells which have been unaffected by the needling.

CHEATLE'S METHOD OF INTERSTITIAL RADIATION

Cheatle's pathological investigations have impressed him with the importance of exposing the whole breast to radiation and not only that part

of it containing the palpable lump. The axillary, supraclavicular, and intercostal regions are radiated in every case, however localized to the breast the disease appears to be.

Cheatle employs the following technique: 80 milligrams of radium element are distributed in 29 needles varying in length as follows:

Needles	Active length centimeters	Each containing milligrams
3	8¼	5
6	7	4
7	6	3
7	4½	2
6	3	1

The ultimate position of the three longest needles is first fixed by inserting them as the central needles of the bottom layer. These needles are placed in position by means of a trocar and cannula. All the needles in the bottom layer are inserted parallel to each other in the posterior part of the breast and irradiate the submammary connective tissue and the upper fibers of the pectoralis major muscle. In the next layer the needles are arranged parallel to each other at right angles to the bottom layer. Whether three layers of needles are inserted depends upon the size of the breast. Lastly the three long needles are passed into the three cannulas which are then withdrawn leaving the needles in position.

In order to help him gage the number of needles and the position they should occupy, Cheatle adopts the following method: The circumference of the breast is measured and marked on a clay surface. Twenty-nine cylindrical blocks of wood, each corresponding in length and circumference to the area of radiation of each of the needles are used. The size of these blocks of wood represents an area of 1 centimeter in all directions. By arranging these blocks of wood, the number of needles, their position, and their distances from one another can be estimated with considerable accuracy.

AUTHOR'S TECHNIQUE

In the attempt to distribute radium bearing needles uniformly throughout a tumor mass, the type of needle best suited for this purpose comes up for consideration. It is at once obvious that the longer the needle the more accurate is the distribution of the radiation. The use of long needles has the distinct advantage that the fewer needles that are used the less chance there is of uneven distribution. The advantages of long needles over seeds are quite obvious.

In view of the radioresistance of most mammary carcinomata, the total quantity of radiation is a significant element in the result. Any factors, therefore, that permit the delivery of a larger dose of radiation to the tumor are important. The three factors that come up for consideration are (1) filtration, (2) the choice of radium element or radon, and (3) the total quantity of radium in relation to the time of exposure.

There is sufficient proof at hand to justify the belief that adequate filtration (0.5 millimeter platinum or its equivalent) is desirable in the treatment of all tumors. It is also very probable that the tumor bed can withstand a larger quantity of adequately, than lightly, filtered radium. There is reason to believe that with adequate filtration, the integrity of the normal breast tissue surrounding the tumor can be better maintained and consequently a larger total dose of gamma radiation may be delivered to the tumor without injury to the tumor bed.

The action of radium element is uniform whereas radon possesses a maximum intensity in the beginning which gradually diminishes with the time of exposure. The intensity of the initial dose is one limiting factor in the total amount of radon that a given tissue can tolerate. The uniform action of radium element has certain advantages in this respect over the uneven action of radon. Whether the difference is of sufficient practical importance to justify the exclusive use of radium element is at present uncertain.

Regaud has claimed that prolonged irradiation over a period of 6 to 8 days has a more marked destructive effect upon a tumor than a similar total dose delivered over a shorter period of time. Aside from this factor, there is considerable evidence to indicate that the toleration of normal tissues is greater when small doses are used over long periods than when a single intensive dose is delivered over a period of several hours. It is logical to believe that in the attempt to deliver a maximum total dose of radiation to a carcinoma in the breast, a larger total dose can be safely delivered when prolonged over 6 to 9 days than can be delivered in a short period of several hours. It would seem, therefore, that the most efficient technique of radiation can be executed by the use of long needles carrying small amounts of radium or radon distributed as uniformly as possible throughout the tumor bearing area and allowed to remain in place for a period of days (6 to 9 days). The author has designed needles for interstitial irradiation as follows:[1]

The needles are constructed in three lengths: 9, 6, and 3.5 centimeters. A gold cylinder with a lumen just large enough to hold glass capillary

[1]The author is indebted to Dr. G. Failla for his aid in designing and constructing the radon needles used in the treatment of these cases.

tubes is encased in a stainless steel jacket. The filtration is equivalent to 0.5 millimeter of platinum. The glass capillaries containing radon are held in place by means of paraffin.

The needles are inserted through the mammary gland and into the lymphatic areas. To the radium needles are attached thin steel wires by which they can be safely withdrawn after having remained in the breast from 7 to 9 days. In placing the needles the main mass of the tumor is avoided, the periphery of the growth being the main objective of the radiation. This technique lessens the danger of dissemination of tumor cells by trauma and prevents the over-radiation of the center of the tumor. The principle of irradiating the periphery of the tumor rather than its center is an important technical consideration that has not been sufficiently emphasized. The center of the growth has a tendency to spontaneous regression and necrosis. Intensive radiation of such an area often results in a complete destruction with central necrosis of tissue. The periphery of the growth is more active and is the zone upon which the radiation must be concentrated. By means of highly filtered, uniformly distributed, accurately applied, and adequate interstitial radiation, it is possible to obtain primary regression and disappearance of mammary tumors which fail to respond to a maximum amount of external radiation.

The technique employed by the writer is based upon the principles of Keynes's method. Radon has been used instead of the radium element. The needles have been made longer in order to insure a more uniform radiation. In the plan of treatment the entire breast is regarded as potentially malignant and the whole gland is irradiated regardless of the size of the tumor mass. The patient receives 1/200 grain scopolomine and 1/6 grain morphine hypodermically 1 hour before operation and a second injection is given when the patient enters the operating room. One per cent novocain is used as a local anæsthetic. The needles are introduced through puncture wounds in the skin previously made with a sharp pointed scalpel. The needles are allowed to remain for 6 to 9 days depending upon the size of the mass. The millicurie value of each needle is approximately 1 millicurie per centimeter length of needle. The total millicurie value employed at one sitting varies between 100 and 130 millicuries. A biopsy of the tumor is performed only in ulcerated lesions or when the clinical diagnosis is in doubt in non-ulcerated lesions. The number of needles employed depends upon the size of the tumor and size of the breast. The needles are placed approximately 1 centimeter apart. Only the periphery of the tumor is irradiated, no needles actually entering the main mass.

REPORT OF CASES

CASE 1. P. W., female, aged 47 years, was admitted to the New York City Cancer Institute on January 30, 1930. The patient had noted a mass on the left anterior chest wall for 2 years. The mass was gradually becoming larger and the overlying skin had recently become thinned and discolored. Examination showed a firm, irregular mass, 6 by 9 centimeters at the base and 4 centimeters high situated at the edge of the upper inner quadrant of the left breast and firmly attached to the chest wall. The overlying skin was markedly thinned, shiny, and purplish red in color. There was impending ulceration. The axillary lymphatic glands and supraclavicular glands were not enlarged.

Treatment. On February 18, 1930, 30 radon bearing needles, each 3.7 centimeters in length and each containing 3.5 millicuries of radon were inserted into the periphery of the growth (see Figs. 1 and 5). The needles were removed after 6 days. The total dose delivered to the tumor was 9150.4 millicurie hours. Regression began immediately and was almost complete after 3 weeks. Two small, discrete tumor nodules at the inner lower quadrant measuring 3 centimeters each remained. In view of the total sterilization of the remainder of the tumor mass, it is believed that these nodules failed to disappear because the needles at that site had lost their radon content during their preparation. On March 25, 1930, 11 needles were inserted beneath the remaining nodules for 6 days. The total millicurie value was 34.36 millicuries. The total dose was 4,507 millicurie hours. The second irradiation was followed by a marked but less pronounced response than occurred after the first irradiation. On June 3, 1930, a third irradiation was performed, 11 short needles each 2.7 centimeters in length being used. Total value 29.8 millicuries for 6 days giving a total dose of 2,620 millicurie hours. The total dose delivered to this tumor during the three treatments was 16,277 millicurie hours. As the axillary and supraclavicular lymphatic areas showed no clinical evidence of disease they were treated with external applications of radium.

The remarkable feature about this case is the perfect recovery of the superjacent skin which appeared to be condemned and the prevention of an impending ulceration. The irradiation of the tumor mass caused a shrinkage and disappearance of the tumor and a collapse of the overlying skin which promptly recovered its normal texture. To avoid ulceration and possible infection, no biopsy was made but the clinical diagnosis is obvious (Fig. 1).

CASE 2. B. C., female, aged 74 years, was admitted to the New York City Cancer Institute on February 17, 1930. The patient first noted a lump in the left breast 3 years before admission. The lump increased in size and became ulcerated 3 weeks previously.

Examination showed an ulcerated lesion 3 centimeters in diameter situated above the left nipple, under which there was a firm nodular mass 8 centimeters in diameter, movable on the chest wall. There was one enlarged axillary node 2 centimeters in diameter; no nodes were felt in the supraclavicular area.

Treatment. Twenty-five radon needles, each 3.7 centimeters in length and each containing approximately 3.5 millicuries of radon, were inserted around the tumor mass for 7 days. The total millicurie value was 81.6 millicuries. The total dose was 58.5 millicuries destroyed or 7,780 millicurie hours. On March 8, 1930, the left axillary node was treated by a surface application of radium at 3 centimeters distance, the dose being 3,000 millicurie hours. On March 22, 1930, a second surface radium application was made; the dose used was 2,500 millicurie hours. On May 6, 1930, the breast tumor had disappeared almost completely leaving a thickened area with a small superficial ulcer in the skin which was slow to heal. This sign was taken as an indication of growth activity and a second radium implantation was performed. Four short radon needles were inserted into this area thus giving a dose of 1,102 millicurie hours, and four long radon needles were inserted into the left axilla giving a dose of 2,832 millicurie hours. On June 14, 1930, a prophylactic surface radiation was performed over the left supraclavicular region (3,000 millicurie hours at 3 centimeters distance).

As Figure 4 indicates there has been complete healing of the ulcerated area and a total disappearance of the breast tumor. The axilla and supraclavicular areas are clinically free of disease. Figure 6 is a photomicrograph of a biopsy specimen taken from the ulcerated edge of the lesion.

SUMMARY AND CONCLUSIONS

1. Because of the radioresistance of mammary carcinoma, interstitial radiation constitutes the method of choice in the treatment of inoperable carcinoma of the breast.

2. Long radium needles that are removable permit a more uniform radiation than can be accomplished by radon seeds.

3. Adequate filtration (0.5 millimeter platinum) is essential in order to effect complete regression of tumors without necrosis.

4. The irradiation of mammary carcinoma must follow the same principle as the radical operation for this disease, i.e., the entire mammary gland and lymphatic areas must be regarded as invaded regardless of the extent of the disease as previously determined by clinical examination.

5. The peripheral or growing edge of a tumor is the most dangerous part of the lesion and requires the most intense radiation. The central portion is poorly nourished, tends to bring about spontaneous necrosis, and requires relatively little radiation.

6. Healing of ulcerated lesions of the breast can be accomplished and impending ulceration prevented by the technique of radiation that has been presented. No claim can be made, however, for the permanency of the results.

7. Peripheral radiation by means of long removable radon needles can accomplish regression of advanced mammary carcinomata which fail to respond to other methods of radiation therapy.

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MALIGNANT TUMORS OF THE KIDNEY IN CHILDHOOD[1]

A Report of Seven Cases of Embryonal Adenosarcoma

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MALIGNANT tumors of the kidney in childhood occupy a special place in renal pathology. They differ from malignant tumors of that organ in the adult in their mode of origin, in their structure, and in their course and clinical picture. It is now generally conceded that most of these new-growths arise from misplaced embryonal rests, and different as they may appear in their gross and histological structure, are mixed tumors having the same origin.

Cohnheim, in 1875, first reported a congenital sarcoma of the kidney which contained striated muscle. He assumed that it had developed from a misplaced mesonephric rest to which a segment of the myotom, which furnished the striated muscle, had become adherent. Weigert, in the next year, reported a congenital adenocarcinoma of the kidney which he believed to have originated from the epithelial renal "anlage." Subsequently numerous reports appeared in the literature of various types of malignant renal tumors in childhood. Some of these were merely designated loosely as sarcoma or carcinoma, while many others were recognized as mixed tumors which differed from one another markedly in their gross and histological structure. They contained epithelium, indifferent round cells, smooth muscle, collagenic and elastic connective tissue, and cartilage in varying amounts.

But in 1896 Birch-Hirschfeld, on the basis of a study of seven specimens and a critical survey of the literature, first discovered the common origin of these neoplasms and placed them in one group. He recognized as the typical new-growth of this class the adenosarcoma, the characteristic feature of which is "epithelial acini occurring in nests of indifferent round cell tissue." He believed the point of origin to be in misplaced rests of the mesonephros, and he called them embryonal glandular tumors (*embryonale Druesengeschwuelste*) or embryonal adenosarcomas.

Because striated muscle is a frequent constituent of these tumors, Wilms placed their point of origin at a much earlier embryonic stage of development. Smooth muscle does occur in the mesonephros, and rests of it are often found in the adult kidney. But unless one assumed a metaplasia of smooth muscle to striated, which Wilms believed could not occur, it would be impossible to explain the development of a striated muscle containing tumor from the mesonephros which contains no striated muscle elements. Hence Wilms believed the origin to be from an early mesodermal rest which has the power of differentiating into sclerotom, myotom and nephrotom. Then the myotom would give rise to the striated muscle, the nephrotom to the glandular complexes, and the sclerotom to the other elements of the tumor.

Ribbert, however, believed that a metaplasia from smooth to striated muscle could occur. He reported a case of "myosarcoma striocellulare of the pelvis and ureter" in which he assumed the striated muscle to have arisen by metaplasia from the smooth muscle of the ureter and the pelvis. In support of this view he demonstrated the presence of transitional muscle forms. Tubulo-epithelial elements were also present and these, he thought, arose from the pelvic epithelium of the kidney.

Busse likewise believed in the possibility of such a metaplasia, and he cited as proof the presence of transitional forms, the arrangement not in bundles but in scattered cells, and the occurrence of striated muscle in other places where only smooth muscle is normally present. As examples of the latter he mentioned tumors of the cervix and vaginal wall in children, and in the uterus following pregnancy. He thought that the embryonal adenosarcomata did not arise from misplaced mesonephric rests because resting non-proliferating islands of the mesonephros have never been found in the kidney. In the case of hypernephromata we have a different situation. Adrenal rests are frequently found in the kidney, and hence the suggestion that tumors might develop from them, as they do from the adrenal gland itself, is justifiable. Busse made sections from the kidneys (metanephros) of 4 and 5 month human embryos and found that the metanephric renal epithelium with its surrounding round cell tissue exactly resembled the "tubulo-epithelial complexes in indifferent round cell tissue" in the embryonal adenosarcomata. He believed, therefore, that these tumors arose from the metanephros, the epithelial complexes from the metanephric epithelium, and the other constituents from the interstitial tissue, either directly or by metaplasia.

[1]From the First Institute of Pathology of the Royal Hungarian Pázmány Péter University in Budapest, Prof. Koloman Buday, Director; and from the Department of Pathology of the Metropolitan St. Stephen Hospital in Budapest, Dozent Edmund De Zalka, M.D., Chief Pathologist.

Trappe and Sand, accepting the theory of Busse speak of these tumors as "malignant embryonal nephromata."

Robert Meyer, following extensive embryological researches, came to the conclusion that various tumors of the male and female urogenital tract originate as the result of an "illegal tissue union" of a mesodermal rest with the wolffian duct. These rests are then compelled by virtue of this union to accompany the duct in all of its migrations and often undergo neoplastic changes.

Lubarsch disputes the possibility of a metaplasia of smooth muscle to striated. He agrees with the theory of Wilms and Robert Meyer as explaining those cases in which striated muscle occurs, and with the theory of Busse for the others.

HISTOLOGY

The predominating histological framework of the typical embryonal adenosarcoma is that of an alveolar sarcoma. Scattered in the indifferent neoplastic round cell nests the epithelial complexes (*Druesenschlauche*, of Birch-Hirschfeld) are found. These epithelial complexes, which are the keynote of these tumors, assume various forms. In some cases the round cells take on an elongated form and an arrangement in rosettes suggesting epithelium. In others the cells are more cuboidal, and they are arranged in tubular acini. While in still others definite cylindrical epithelium with a well defined basement membrane is found. The epithelium may in some cases undergo a proliferation forming compact epithelial nests and suggesting medullary carcinoma. Cysts may also develop as well as structures resembling glomeruli. In each case the round cells and epithelial cells are highly hyperchromatophilic, and mitoses are frequent. If one examines the nests of round cells with their contained epithelial complexes, "the tubulo-epithelial complexes in nests of indifferent round cell tissue," under oil immersion, one sees fine strands of connective tissue coursing among the round cells. Accompanying these delicate fibers are small capillary blood vessels.

The coarser framework supporting the alveolar round cell nests is made up mainly of collagenic connective tissue. Smooth muscle fibers are very frequently placed among the connective tissue fibers and are recognized by their long, blunt ended nuclei and their yellow color with the Van Gieson stain. Elastic fibers are also occasionally seen.

Most interesting are the striated muscle fibers which are also frequently seen. They usually occur not in bundles but scattered among the connective tissue fibers. The sarcolemma is usually absent, and tubular forms are frequent. Fusiform cells in which no striations are visible, but which take the Heidenhain iron-hematoxylin stain, occur. According to Wilms, striated muscle occurs in about 40 per cent of these tumors. Myxomatous connective tissue, fat, and cartilage may be present in this coarser supporting framework.

GROSS PATHOLOGY

Grossly the embryonal adenosarcomata have a characteristic appearance. They are usually the size of a large orange, a grapefruit or larger, and are well encapsulated from the surrounding renal tissue. On cut section the predominating cast is gray, but due to necrosis and hæmorrhage, various shades of red and brown occur. Hyaline connective tissue and cartilage may show areas of glistening white, producing a varicolored appearance. Cysts filled with a stringy mucoid material may be present, so that when cut a viscid fluid clings to the knife. These tumors are often very brittle, and when relieved of the restraining influence of the capsule by cutting, they may fall to pieces. The neoplasm is usually on the lower pole of the kidney and grows from within out, compressing the surrounding renal tissue which undergoes degeneration and helps to form the capsule. The tumor often grows into the renal pelvis completely occluding it. Here it often takes on a papillary form.

MODE OF GROWTH

The mode of growth is usually not infiltrating but crowding, the tumor being well restrained by its capsule. At first, while the neoplasm is still small, the renal tissue is pressed aside and undergoes atrophic changes, being stretched peripherally by the rapidly growing mass. Finally it forms a mere shell which fuses with the capsule of the tumor. The surrounding tissues are gradually pushed aside by a process of crowding. Adhesions to the periphery are usually absent. The colon is at first dislodged anteriorly and lies in front of the tumor. It is then pushed medially as the size of the neoplasm increases. The liver and the diaphragm are then gradually dislodged upward, and the lower thoracic wall begins to bulge. Finally the entire abdomen is filled.

The growth is extremely rapid, large tumors having been found in the newborn and even in fetuses, while a growth scarcely appreciable at birth may increase to such size within a few months time as to fill completely the abdomen.

METASTASES

Metastases occur mainly by way of the blood stream, the most frequent sites being the liver and

the lungs. The osseous system and the lymph nodes are usually spared. Neoplasms of the kidney, in general, because of the structure and the rich vascular supply of that organ are especially prone to metastasize by way of the blood stream.

Occasionally the embryonal adenosarcomata spread to the surrounding organs by way of the lymph channels. But this occurs usually only after the tumor has attained a very large size and has broken through its capsule. At that stage local infiltration of the surrounding tissues and adhesions may also occur. The metastases may either resemble the original tumor, or only one or more of its constituents may be present as in other mixed tumors. They usually occur late.

OCCURRENCE OF THE ATYPICAL FORMS

Malignant renal tumors in children are often carelessly described as rhabdomyoma, sarcoma, carcinoma, myxoma, etc. As a matter of fact they are mostly, as Birch-Hirschfeld first suggested, mixed tumors and belong to the embryonal adenosarcoma group. The embryonic rest from which they arise is very undifferentiated and very rapidly growing (*in lebhafter Wucherung begriffen* —Birch-Hirschfeld). As a result, certain tissues may grow more rapidly than the others, and possessing a greater proliferative power and resistance, may crowd the others out of existence and destroy them. Thus by a battle of the tissues (*Gewebskampf*—Askanazy) and a survival of the fittest, one tissue type may command the field and make up the major or even the entire part of the growth. So a tumor beginning as an embryonal adenosarcoma, by the eccentric development of one of its constituents, may end up as a rhabdomyoma, a myxosarcoma, a fibrosarcoma, a round cell sarcoma, or a carcinoma. This is amply demonstrated in the pure enchondromata of the parotid and the strumas of the ovary, which are really mixed tumors. Pure rhabdomyomata of the kidney never occur. They are all mixed tumors and so with most of the sarcomata and carcinomata of the kidney in childhood. In most of these tumors, as Borst, Hedrén, Birch-Hirschfeld, and Wilms have shown, a careful and extensive search will reveal a few of the typical round cell and epithelial (adenosarcoma) complexes described by Birch-Hirschfeld.

FREQUENCY OF OCCURRENCE, AGE AND SEX INCIDENCE

In 1924 Lubarsch was able to collect from the literature 137 cases of embryonal adenosarcoma. Of these 52 occurred in females, 66 in males, and in 19 the sex was not indicated. In 55 cases the neoplasm was on the right side, in 50 on the left side, and in 6 the neoplasm was bilateral. In 25 the side was not indicated. The age incidence was as follows:

Age in Years	Cases	Age in Years	Cases
Fetuses and newborn	4	9	5
1	18	10	1
2	24	11	1
3	25	12	2
4	18	14	1
5	13	15	1
6	6	19	1
7	4	23	2
8	4	35	1
		57	1

In 5 cases the age was not indicated. So it is seen that most cases occur within the first 5 years of life, but cases have been reported as late as the fifty-seventh and the seventy-second year of life.

CONGENITAL FEATURES

The most striking evidence of the congenital nature of these tumors is their not infrequent bilateral occurrence. Associated developmental defects may also exist, as in the case of Weigert, in which, in addition to a bilateral renal tumor, bilateral undescended testes, hare-lip, and cleft palate were also present. Further the neoplasm may occur in several members of the same family, as in the case of Walker in which a brother and sister were thus affected and the case of Struempell (cited by Walker) in which two brothers were afflicted with renal "sarcoma."

SYMPTOMATOLOGY

The most striking symptom of malignant renal tumors in childhood is a large, rapidly growing abdominal tumor unaccompanied by pain or hæmaturia. The patients seem to be in fairly good health except for the presence of the abdominal mass. As the tumor assumes larger proportions, cough may set in. This is unusually reflex or due to mechanical causes, but it may be the result of pulmonary metastases. Bladder symptoms are usually absent. Diminution or complete suppression of urine may result from compression of the ureter of the opposite side. Fever is present more often than in the renal tumors in the adult due to the rapid growth of the neoplasm and the unstable temperature mechanism in children. Gastro-intestinal symptoms such as constipation or diarrhœa may occur, but usually very late in the course of the disease. It is amazing how often a huge tumor filling half of the abdomen and dislocating the entire peritoneal cavity to the opposite side produces no symptoms on the side of the gastro-intestinal tract. According to Albarran

and Imbert hæmaturia occurs as an early symptom in only 5 to 15 per cent of the cases. It is because of this absence of other signs, especially of the alarming hæmaturia which brings the adult patient so early to his physician, that these little patients come to the surgeon so late. Hence the poor prognosis in the operative result.

DIAGNOSIS

The diagnosis is usually made readily by palpation of a large abdominal mass. One should in this connection bear in mind that many of the large abdominal tumors in childhood are malignant renal tumors. Hydronephrosis may cause difficulty, but this is usually ruled out by the different degrees of filling at various times.

THERAPY

Most surgeons (Israel, Voelcker, and others) agree that these cases should be operated upon, regardless of the size of the tumor, if metastases or severe cachexia are not present. Unless this is done, the child will die within a year after the tumor is discovered. The youth of the patient is not a contra-indication. Israel reports a successful operation in a 3½ month infant in which a tumor filling two-thirds of the abdomen was removed. In a case reported by Abbe, a 7½ pound tumor was removed from an 8 month child with recovery. Kynoch (quoted by Hedrén) reports 7 cases successfully operated upon in young children.

Operative approach. Israel favors the retroperitoneal approach, the line of incision following the long axis of the tumor. Voelcker's incision begins in the costovertebral angle and extends to the umbilicus. He opens the peritoneum widely. It seems, however, that the midline laparotomy incision which was used in the cases here reported, and which is favored by most operators, including Albarran, is the best, as it enables one better to explore the abdomen for metastases (liver, mesenteric nodes, etc.) and to determine if the tumor is bilateral. In either case one can immediately close and avoid subjecting the patient to an unnecessary operation. Israel and Voelcker both warn against mass ligatures of the renal pedicle, and advise careful exposure of the large vessels. Because of the flexibility of the tissues in the child, the vena cava and opposite renal vein can very readily be pulled over and caught in the clamp, as in one case reported by Voelcker. In using the midline laparotomy incision one should always keep in mind the displacement of the peritoneum by the huge tumor. Thus in Abbe's case, the peritoneal cavity was so far dislocated to the right by the left sided growth that a midline laparotomy incision brought him down on the tumor extraperitoneally (Fig. 28). If careful hæmostasis is carried out, the smallest child will stand the operation well.

Many of these patients are operated upon merely on the diagnosis of abdominal tumor. Hence cystoscopy is often not done. It is alarming how frequently such a kidney is removed without a previous examination to assure the presence and adequate function of the other organ. Since these tumors are the result of a congenital malformation, other congenital defects, such as congenital absence of the other kidney, may be present. Hence at least chromocystoscopy should be done in every case, except in very young male children where intravenous pyelography will serve as well. Cystoscopic pyelography is usually unnecessary because the other clinical findings are typical.

PROGNOSIS

In a series of 20 cases not operated upon followed by Albarran and Imbert, 14 died within 6 months, 3 within one year, 3 after 1½ years, and only 1 survived 3 years. Deaths due to recurrences and metastases after operation usually occur within the first year, but they may occur as late as the fifth. Hence Israel advises a 5 year period of observation before pronouncing a cure. The operative mortality, according to Albarran and Imbert is about 25 per cent, while the total early and late mortality including deaths due to recurrences and metastases reaches 86 per cent.

REPORT OF CASES

CASE 1. B. M., a girl, 9 months of age. The family history was negative. Delivery was normal and she weighed 4000 grams at birth. The developmental history was negative. During the past month the parents have noticed a rapid increase in the size of the abdomen. There was no hæmaturia, pain, or other symptoms or signs.

Physical examination. The child weighed 8150 grams. The skin had a poor turgor. The head, neck, extremities, heart and chest, and superficial lymph nodes were negative. The left side of the abdomen was enlarged. A tumor the size of a child's head was palpable in the left flank. It was readily ballottable and extended under the costal arch and to the midline in front. X-ray examination showed the diaphragm pushed up on the left and the liver dislocated to the right. The red blood count was 3,540,000; white count 7,000. Temperature was 99.2 degrees. June 23, an operation was done under chloroform anæsthesia: a midline laparotomy, by Dozent Dr. Koos. A large left sided retroperitoneal tumor attached to the left kidney was removed. The ureter and the renal vessels were readily tied off. Recovery followed with primary healing of the wound.

Histology (Figs. 11, 12, 18, and 19). The tumor consisted mainly of nests of indifferent round cell tissue in a coarse, supporting connective tissue framework. The round cell nests contained groups of low cuboidal and cylindrical epithelial cells arranged in well defined acini.

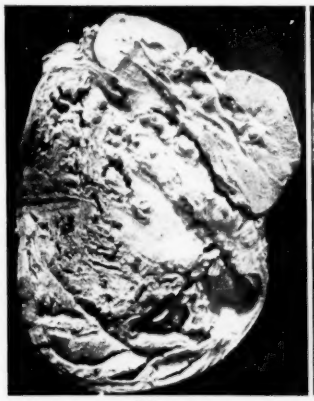


Fig. 1.

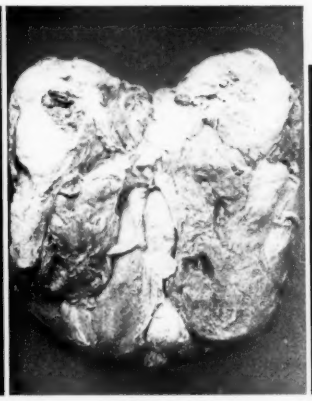


Fig. 2.

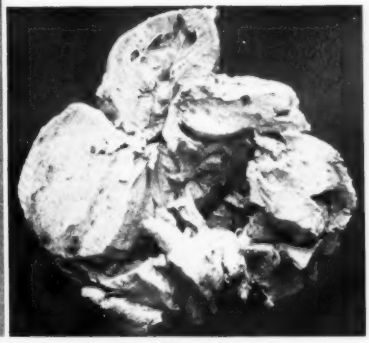


Fig. 3.

Fig. 1. Embryonal adenosarcoma, Case 2. The tumor lies on the lower pole of the kidney, which has been destroyed by the growth. The tumor has a well defined capsule.

Fig. 2. Embryonal adenosarcoma, Case 3. Only the upper pole of the kidney remains. The tumor has completely filled the pelvis.

Fig. 3. Embryonal adenosarcoma, Case 4. The friable white tumor mass lies on the lower pole of the kidney, the upper pole of which is hydronephrotically dilated.

Both round and epithelial cells showed many mitoses. The supporting framework contained collagenic fibers, fibroblasts and a few smooth muscle cells. Striated muscle fibers were present in large numbers, diffusely scattered. Tubular forms and spindle shaped forms were also present. There was no sarcolemma. Elastic fibers were not present except in the capsule. Small areas of necrosis and hæmorrhage were noticeable.

Case 2. F. I., a girl 2½ years old. The family history was negative. The child was a 7½ months premature infant. Previous history was negative except for varicella at 1½ years of age. For the past 3 weeks the parents have noticed a rapid increase in the size of the abdomen. There was no pain, no hæmaturia, and no gastro-intestinal symptoms.

Physical examination disclosed a moderately well developed child. The head, neck, heart, lungs, extremities, and superficial lymph nodes were negative. The left half of the abdomen was enlarged. A mass the size of a child's head was palpable in the left flank. It just reached the costal arch above and the midline anteriorly. It was readily ballottable. On January 4, under ether anæsthesia, Dozent Dr. Koos did a midline laparotomy. A tumor the size of a child's head and attached to the left kidney was removed from the left retroperitoneal region. The ureter and renal vessels were readily tied off. January 5, patient developed a left lower lobar pneumonia. January 10, the wound broke open in its entire length. January 15, the wound was granulating nicely; the patient had a normal temperature. January 26, patient was discharged from the hospital.

Gross pathology (Fig 1). The tumor lay on the lower pole of the kidney and measured 12 by 9 by 6 centimeters. It had a thick, well defined capsule which fused with the capsula propria of the kidney. The lower pole of the kidney had been destroyed by the tumor, the upper and medial half of which was composed of a white, papilloma-like friable mass. The lower and lateral half was made up of a firmer, lamellated tissue which contained shades of browns and reds due to hæmorrhage. The ureter, pelvis, and calyces were fairly intact.

Histology (Figs. 7, 9, 10, 13, and 20). There were nests of indifferent round cell tissue containing epithelial cell groups in rosette forms, and as cuboidal and cylindrical epithelium, in the form of well defined acini. Glomerulus like forms were present. Fine connective tissue fibers appeared among the round cells. Supporting the round cell nests was a coarse framework of collagenic fibers, fibroblasts, smooth muscle, and a few small areas of loose, œdematous connective tissue. A few striated muscle fibers, including tubular and fusiform types, were also present. A few scattered elastic fibers were present in the stroma and in the capsule.

Case 3. A boy 2 years old. The history was not obtained in this case.

Gross pathology (Fig. 2). The tumor was situated on the lower pole of the kidney with which it measured 12 by 6 by 6 centimeters. Only the upper pole of the kidney remained. The tumor was walled off from the periphery by a well defined capsule which fused with the capsula propria of what remained of the kidney. The tumor presented areas of elastic consistency, white in color, and other areas which were more grayish yellow, and were softer and more brittle (necrosis). In the center was a hen's egg sized area of very brittle, spongy, necrotic tissue infiltrated with blood and containing large clots. The tumor had broken into and completely filled the pelvis as a solid mass, compressing and infiltrating the renal parenchyma which it had perforated, and presented on the external surface as a cherry sized mass. A large portion of the pelvis and the upper portion of the ureter had been destroyed.

Histology (Figs. 6, 16, 22, 23, and 24). There are nests of round cells with only an occasional grouping of cells to suggest epithelium. A coarse supporting framework contained collagenic fibers, fibroblasts, and smooth muscle. Striated muscle was not seen. Elastic fibers were present in some of the large septa. Fat tissue was also present. Areas of necrosis and hæmorrhage were found. The renal parenchyma was compressed, the tubules had disappeared and the glomeruli were closely packed together.

Case 4. S. T., a 4½ year old boy. A history was not obtained. The child was operated upon by Dozent Dr. Koos.

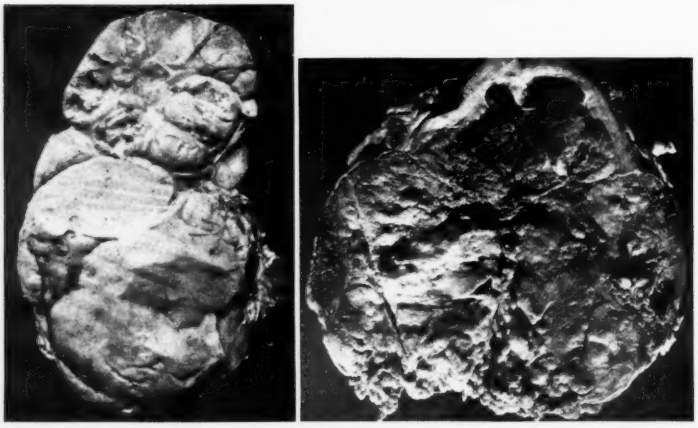


Fig. 4, left. Embryonal adenosarcoma, Case 5. The white tumor mass is composed of two spherical parts and lies on the medial aspect of the kidney which thins out above and below to fuse with the tumor capsule.

Fig. 5. Embryonal adenosarcoma, Case 7. The tumor lies on the lower pole of the kidney and fills all of the pelvis except the upper calyx which is dilated. The villous structure is well shown.

for right sided renal tumor. A midline laparotomy was made under ether anæsthesia.

Gross pathology (Fig. 3). The tumor measured 14 by 10 by 9 centimeters, and lay on the lower pole of the kidney. It was made up mainly of a fairly homogeneous, brittle, white mass presenting areas of gray (necrosis), brown, and red (hæmorrhage). A well defined capsule, which fused with the capsule of the kidney, was present. The pelvis and calyces were hydronephrotically dilated and the papillæ were flattened. The ureter could be followed as a compressed strand in the capsule of the tumor.

Histology (Figs. 8, 14, 15, 17, and 21). Nests of round cells contained epithelial groups in all stages of transition from rosette forms to cylindrical epithelium. Glomerulus-like forms were present. Many mitoses were noted. The supporting framework was mainly a loose connective tissue with scattered fibroblasts, round cells, wandering cells, and in many places considerable œdema was noticeable. Many star-shaped fibroblasts were present causing the tissue to resemble myxomatous connective tissue. There were occasional smooth muscle cells, mainly around the round cell nests. A few, not completely developed, striated muscle fibers and a few elastic fibers were present. Large areas of spindle cell tissue showed many mitoses. There were areas of necrosis and hæmorrhage.

Postoperative course. The tumor recurred at the site of extirpation and the child died 4 months after the operation. Autopsy showed extensive recurrence of the tumor tissue at the site of extirpation and metastases in the abdominal lymph nodes and liver. The histologic structure was essentially that of the primary tumor except that striated muscle fibers were not present. Glomerulus forms are well developed.

CASE 5. G. L., boy of 12 months. Family, birth, and developmental history were negative. The parents noticed a rapid growth in the size of the abdomen for one week. No hæmaturia, no pain, no other symptoms or signs were present. Bowels were in order.

Physical examination. The skin showed a good turgor; the subcutaneous fat was fairly well developed. The head, neck, heart and lungs, extremities, and superficial lymph nodes were negative. In the right side of the abdomen an orange sized, moderately hard mass was palpable. It extended up under the liver and medially beyond the midline. Temperature was 100.4 degrees. On August 5, Dozent Dr. Koos removed, through a midline laparotomy and under ether anæsthesia, a tumor the size of two oranges. The tumor was attached to the right kidney and was in the right retroperitoneal region. The tumor was not adherent to the periphery or to the peritoneum. Convalescence was uneventful except for a complicating varicella. Patient was discharged from the hospital September 3, with primary healing of the wound.

Gross pathology (Fig. 4). The tumor lay on the medial and lower side of the kidney and measured 13 by 6 by 8 centimeters. It was composed of two spherical parts, a smaller upper, divided by thin, glistening white connective tissue septa into pea to cherry sized nodules of fairly elastic consistency; a lower, larger, homogeneous, white mass of elastic consistency. The remains of the kidney thinned out above and below to fuse with the well developed capsule of the tumor. The ureteropelvic juncture and ureter disappear in a mass of tumor tissue which compresses the renal pelvis.

Histology. There were round cell nests containing epithelial groups composed of cuboidal epithelium; many glomerulus forms. No elastic tissue or striated muscle was present.

CASE 6. Girl, 6 months old. For the past week and a half the parents have felt a mass in the right side of the abdomen. There was no hæmaturia and apparently no pain.

Physical examination revealed a well nourished, well developed female child, who weighed 5,300 grams. The skin had a good turgor; there was no œdema. The abdomen was distended and somewhat asymetrically enlarged, being somewhat more prominent on the right side. Under the right costal margin a firm ballottable mass of elastic consistency and somewhat larger than an apple was palpable. On the left side there was a somewhat smaller, immovable mass near the umbilicus. The urine contained a large

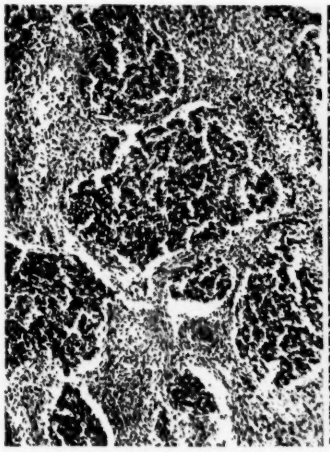


Fig. 6.

Fig. 7.

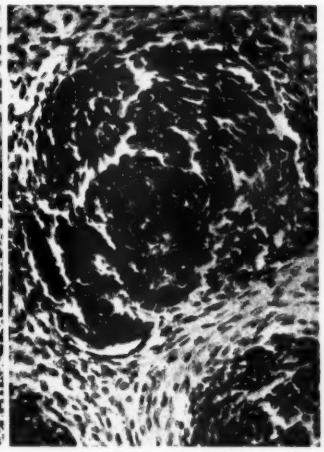


Fig. 8.

Fig. 6. Low power photomicrograph showing nests of indifferent round cell tissue in connective tissue framework resembling alveolar sarcoma (Case 3).

Fig. 7. Low power photomicrograph showing nests of indifferent round cell tissue containing epithelial cell groups. This is the typical picture of the embryonal adenosarcoma (Case 2).

Fig. 8. High power view of round cell nests showing the assumption of an oval form by the cells and the arrangement in rosettes resembling epithelium (Case 4).

Fig. 9.

Fig. 10.

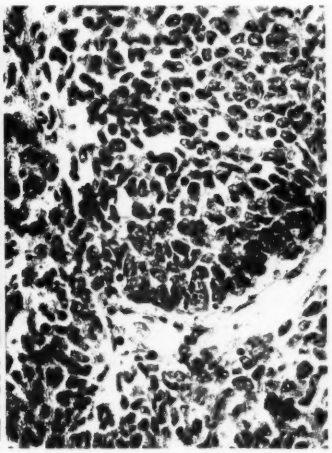


Fig. 11.

Fig. 9. High power view of round cell nests. The cells have here developed into a well defined cuboidal epithelium forming an acinus with a well defined lumen. Rosette forms are also seen (Case 2).

Fig. 10. High power view of round cell nests showing well defined cylindrical epithelium (Case 2).

Fig. 11. High power view showing development of epithelial cells into compact cell groups with hyperchromatophilia and many mitoses, somewhat resembling medullary carcinoma (Case 1).

quantity of albumin and many red blood cells. There were 2 leucocytes per high power field. The white blood count was 8,900 and the red count 3,480,000.

On June 11, an abdominal palpation was done under chloroform anæsthesia. June 12, the temperature rose to 104 degrees; the respirations were 42. The child was cyanotic and there was considerable dyspnœa. Crepitant râles were audible over both lungs. Death occurred at 6 p.m.

Autopsy findings. Both kidneys were considerably distorted and largely replaced by a soft, white, friable tissue. It had a nodular structure, the largest nodules being the

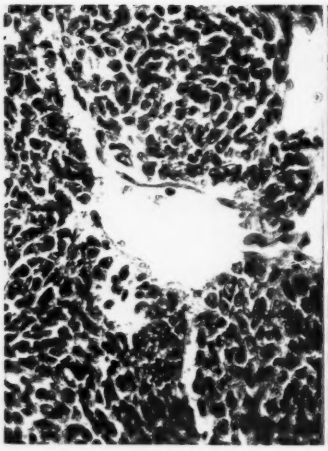


Fig. 12.

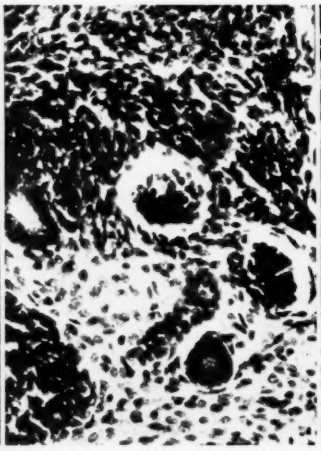


Fig. 13.

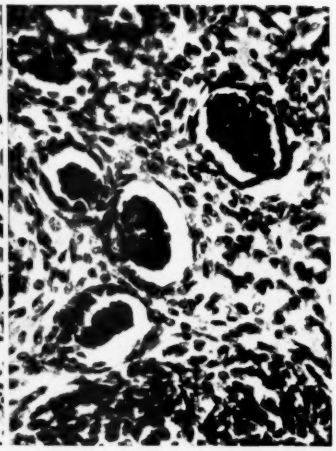


Fig. 14.

Fig. 12. High power view showing area of tumor resembling medullary carcinoma (Case 1).

Fig. 13. High power view showing structures resembling incompletely developed glomeruli (Case 2).

Fig. 14. High power view showing structures resembling more completely developed glomerulus forms. These are, however, not as yet identical with fully developed glomeruli (Case 4).

size of a walnut. On the right side only a very small rest of kidney tissue remained on the lower pole. The rest of the organ had been replaced by the tumor mass, which was the size of an apple and which was well restrained by a well defined capsule which fused below with the capsula propria of what remained of the kidney. The left kidney was dumbbell shaped. There were two tumor masses the size of a hen's egg separated by a narrow bridge of compressed kidney tissue. A very small rest of kidney tissue remained on the lower pole. The entire mass was restrained by a well defined capsule. Grossly the neoplastic tissue appeared to be identical on both sides.

No metastases were found. There was apparently very little displacement of the abdominal organs. The ascending colon lay anterior to the right kidney. The lungs showed a congestive hyperæmia.

Histology. There were round cell nests containing epithelial groups in the form of rosettes and of well defined epithelium. Glomerulus forms were noted. The supporting framework contained collagenic connective tissue and smooth muscle, but not striated muscle. Necrosis and hæmorrhage were seen.

CASE 7. K. M., 7 year old girl. Family and previous history were negative. The parents noticed a rapidly growing mass in the right flank of 3 months' duration. During this time the child had also complained of some pain. There was no hæmaturia at any time, no fever, and no other symptoms.

Physical examination revealed a moderately well developed female child. The head, neck, heart and lungs, extremities and superficial lymph nodes were negative. There was a slight protuberance of the right side of the abdomen. In the right flank a ballottable mass filling the right side of the abdomen was palpable.

On the suspicion of renal tumor, chromocystoscopy was done and a normally functioning kidney was demonstrated on the left side.

Operation was done under ether anæsthesia through a midline laparotomy, by Dr. Lévai. A large tumor connected to the right kidney was removed from the right retroperitoneal region. The patient was discharged with the wound healed.

Gross pathology (Fig. 5). The tumor mass lay on the lower pole of the kidney and measured 16 by 9 by 6 centimeters. A more or less homogeneous, soft, friable, brownish, papilloma-like tissue with cherry-sized and smaller villi comprised the growth. Occasional strands of glistening white connective tissue ran through the mass. There were scattered areas of necrosis and hæmorrhage. The tumor had broken into the renal pelvis filling all of it except the upper calyx which was hydronephrotically dilated. It had spread apart the lower part of the kidney parenchyma, which thinned out below to fuse with the thick, well defined capsule of the tumor. The lower part of the pelvis and the upper part of the ureter were completely destroyed.

Histology (Fig. 25). The supporting framework contained mainly collagenic connective tissue and smooth muscle. The round cell nests contained very little indifferent round cell tissue but mainly "epithelial" groups. The lumina of the acini were lined by a homogeneous membrane around which the cells were in most cases arranged in several layers. The nuclei were well seen and many mitoses were present. The cytoplasmic borders were not very distinguishable. The arrangement somewhat resembled that which is present in endothelioma (Fig. 25). In a few cell groups, however, well defined cylindrical epithelium was seen. No striated muscle was present and there were found only a few scattered elastic fibers in the stroma.

NOTE.—Cases 1, 2, 4, and 5 are from the service of Dozent Dr. Koos of the Stephany Children's Hospital, Budapest. Cases 3 and 6 are from the pathological service of Dozent Dr. de Zalka of the same hospital. For Case 7, which is from the Industrial Hospital of Budapest, I am indebted to Adjunct Dr. Nachtnebel of the first pathological institute of the Royal Hungarian University at Budapest.

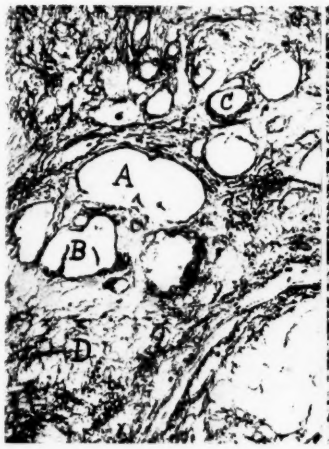
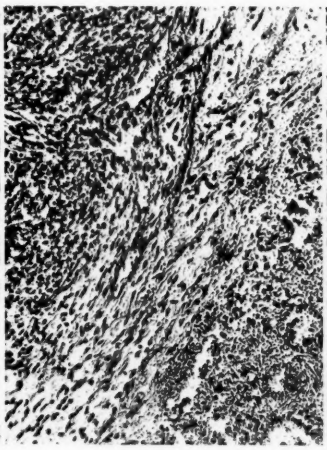


Fig. 15.



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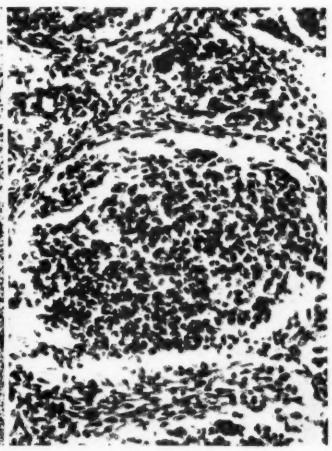


Fig. 17.

Fig. 15. High power view showing the fine connective tissue or true stroma of the "indifferent round cell nests" of the embryonal adenosarcomata. The empty spaces *A* and *B* represent epithelial tubules, *C* a blood vessel, and *D* and *E* the fine connective tissue fibers lying among the indifferent round cells. Bielschowsky-Maresch impregnation (Case 4).

Fig. 16. Low power view of connective tissue framework showing, upper left, spindle cell sarcomatous tissue, in the middle collagenic fibers and fibroblasts; and in the lower right an area of necrosis with a few tubules still visible (Case 3).

Fig. 17. Low power view of round cell nest and supporting framework. Arranged in a circle around the nest are many smooth muscle fibers, recognized by their long, blunt ended nuclei (Case 4).

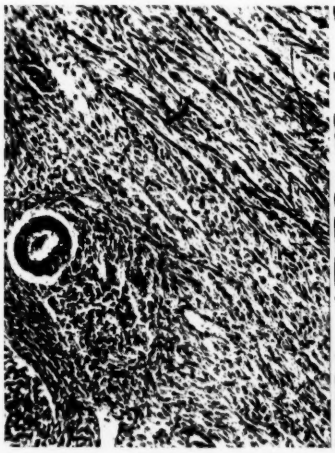
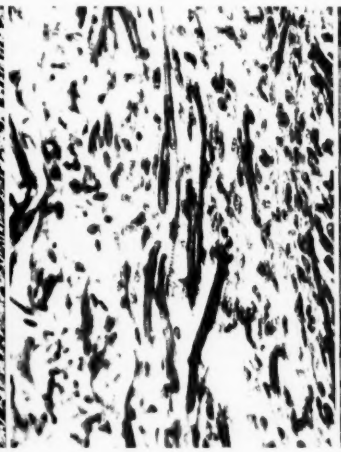


Fig. 18.



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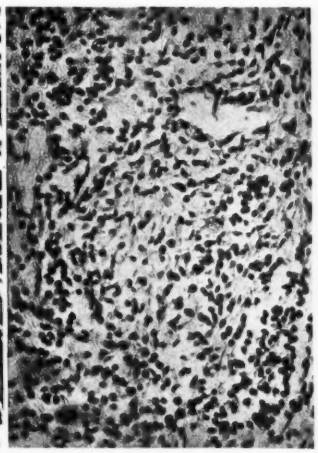

Fig. 20.

Fig. 18. Low power view showing in the upper right hand corner numerous striated muscle fibers. Heidenhain iron hæmatoxylin stain (Case 1).

Fig. 19. High power photomicrograph of area shown in Figure 18, showing well defined striated muscle, including fusiform and tubular forms. The fibers are scattered, and there is found no sarcolemma. Heidenhain iron hæmatoxylin stain.

Fig. 20. High power view of tumor showing loose œdematous connective tissue (Case 2).

DEDUCTIONS

Whereas the typical embryonal adenosarcoma shows a typical histologic structure, the atypical and aberrant types may lead us into difficulty.

Ribbert claims to have seen in these tumors neuro-epithelium, such as occurs in mixed tumors of the testicle, while other authors report ciliated epithelium. Wilms doubts if these forms ever occur. They were not seen in our cases.

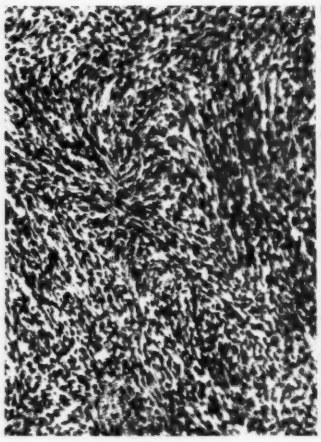

Fig. 21.

Fig. 22.

Fig. 23.

Fig. 21. Low power view of spindle cell sarcomatous tissue with many mitoses (Case 4).

Fig. 22. Low power view showing elastic fibers in supporting framework of tumor. Weigert's resorcin fuchsin stain (Case 3).

Fig. 23. Low power view. Fat tissue in tumor (Case 3).

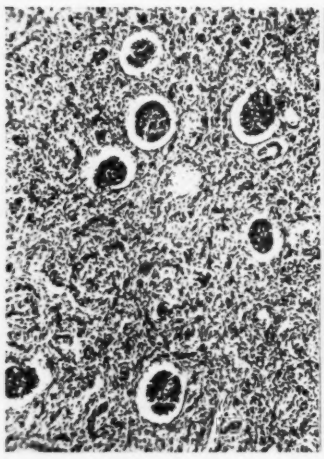

Fig. 24.

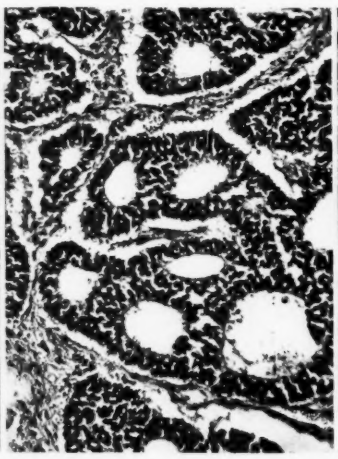

Fig. 25.

Fig. 26.

Fig. 24. Low power view showing the compressed renal parenchyma. The tubules have already disappeared. The glomeruli are closely packed together and have not as yet undergone degeneration (Case 3).

Fig. 25. High power view showing an arrangement of cells somewhat resembling the arrangement in endothelioma (Case 7).

Fig. 26. High power view of the cortex of the kidney of a 14 centimeter human embryo showing the metanephric tubules lying in a group of as yet undifferentiated round cells. The picture bears a striking resemblance to the "epithelial cell groups in nests of indifferent round cell tissue" of the embryonal adenosarcomas. (For comparison see Figs. 7, 8, 9, and 10.)

Birch-Hirschfeld considered the tubulo-epithelial groups and the surrounding indifferent round cell tissue to exist not in the relation of tumor parenchyma and tumor stroma, but to be both of epithelial origin. He referred to the round cells as archiblastic cells and believed that they could develop into epithelial cells. The work of Hedrén in which he demonstrated in serial sections a gradual transition from the surrounding indifferent round cells to the epithelial tubules supports this view, and also the various stages of development from mere rosettes to well defined

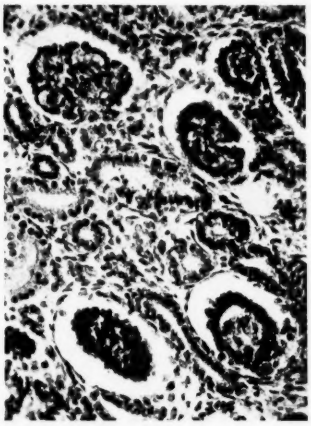

Fig. 27. High power view of another area of the cortex of the same kidney as is shown in Figure 26. Glomeruli in various stages of development are seen. The structure in the upper left hand corner represents a fairly well developed glomerulus with capillary loops well filled with blood. The others represent earlier stages (pseudo-glomeruli) and closely resemble the glomerulus forms of the embryonal adenosarcomata. For comparison see Figures 13 and 14.

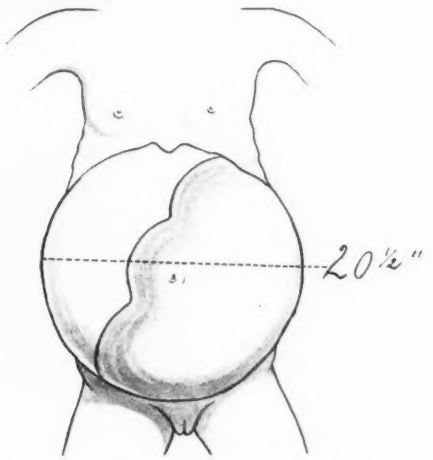

Fig. 28. Sketch showing dislocation of the peritoneal cavity by a huge renal tumor in a 7 months' child. A midline laparotomy incision exposed the mass extraperitoneally. (Case of Abbe.)

epithelium, which all observers report. We have seen these various stages repeatedly in our cases, as Figures 8, 9, and 10 demonstrate. Birch-Hirschfeld considered the true stroma of the round cell nests with their included epithelial groups to be the fine connective tissue fibers with their blood supply which lie among the indifferent round cells. In our cases we have demonstrated this tissue with the aid of the Bielschowsky-Maresch impregnation method, as demonstrated in Figure 15. We have also examined histologically the kidneys (metanephros) of human embryos 7, 8, 9, 10, 14, 22, and 26 centimeters in length. In these, just as Busse found, the renal tubular parts were made up partly of undifferentiated round cells and partly of well defined epithelial cells exactly resembling the "round cell nests containing tubulo-epithelial cell groups" of the embryonal adenosarcomata; (see Fig. 26). This finding strongly supports the theory of the metanephric origin of the embryonal adenosarcomata. Glomeruli in various stages of development were also seen, some exactly resembling the glomerulus-like forms of the tumors, as in Figure 27. Most authors, while admitting the resemblance of these structures to glomeruli, look upon them as eccentric proliferations of the tubulo-epithelial parts of the tumors and express some doubt as to whether they actually represent glomeruli. Kaufmann suggests that postembryonic development of glomeruli does not occur. But in this connection, I believe we must not forget that these tumors represent embryonic tissue. Weigert, in 1876, reported a case of bilateral congenital adenocarcinoma in a stillborn infant. This case is, according to our view, a typical adenosarcoma, as the histological description and the accompanying illustrations prove. Glomerulus-like forms were present. Weigert considered them to be embryonic glomeruli and identical in structure with the pseudo-glomeruli which Toldt saw in his studies on the development of the kidney. These latter structures result from an eccentric proliferation of the embryonic renal tubular epithelium and represent a transitional form to the development of the true glomerulus.

As to the origin of these tumors, as we have already stated above, they undoubtedly represent metanephric tissue. The question as to whether they arise from the already differentiated metanephros itself (theory of Busse) or from a mesodermal rest containing metanephric "anlage" or nephrotom, as Wilms believes, may still be left open to discussion. If one accepts the possibility of a metaplasia of striated from smooth muscle, the theory of Busse might explain all cases. But such a metaplasia has never been proved. So we would be compelled to accept the theory of Wilms which places the origin of the striated muscle cells in these tumors from the myotom portion of the mesoderm. But, as is known, only about 40 per

cent of these tumors contain striated muscle. *We therefore believe that the neoplastic proliferation of the metanephros may occur at any stage in its development from the mesodermal stage, where, in addition to the metanephric "anlage," striated muscle "anlage" or myotom is present, to the stage where actual metanephros has differentiated and striated muscle "anlage" is no longer present. Hence the earlier origin (theory of Wilms and Robert Meyer) could be ascribed to those cases where striated muscle is present and the later origin to those cases where it is absent.*

The high total early and late mortality (86 per cent) of malignant tumors of the kidney in childhood is not so amazing when we compare this figure with that of malignant renal tumors in the adult (70 to 80 per cent). Especially so when we consider how late these children usually come to the surgeon, due to absence of alarming symptoms and the rapid growth of the neoplasm.

SUMMARY

1. Most large abdominal tumors in childhood are malignant tumors of the kidney.

2. Most malignant tumors of the kidney in childhood are mixed tumors of the embryonal adenosarcoma group.

3. An extensive histological study of every case of renal tumor in childhood is urged. Sections should be taken from every part of the neoplasm and a careful search made for the typical epithelial groups which will identify the tumor as an embryonal adenosarcoma. The failure to demonstrate these epithelial groups does not exclude the possibility that the tumor belongs in this group.

4. The embryonal adenosarcomata arise from the metanephros. The neoplastic change of the latter may occur at any stage in its development from the mesodermal stage, where it is present only as metanephric "anlage," to the point where actual metanephros has already differentiated. The earlier origin may be ascribed to those cases in which striated muscle is present and the later origin to those cases where it is absent. The glomerulus-like structures in these tumors represent true embryonic glomeruli.

5. The most outstanding symptom of malignant renal tumors in childhood is usually a rapidly growing, painless abdominal tumor. Hæmaturia is usually absent.

6. The midline laparotomy incision is preferred.

7. Cystoscopic study of every case is urged to assure the presence of a functionally efficient kidney on the other side. In very young male children intravenous pyelography may suffice.

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RADIATION THERAPY OF CARCINOMA OF THE BLADDER

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THE purposes of this paper are (1) to describe the methods of treating cancer of the bladder at the Memorial Hospital, (2) to present an analysis of the radiation furnished by the use of radium and the roentgen-rays, and (3) to present results following radiation therapy.

Before undertaking the treatment of any bladder cancer it should be classified as to form, size, location, histological structure, amount of infiltration, and the presence or absence of metastases. This information may be obtained by rectal palpation, cystoscopic examination, a biopsy from the base of the growth, and stereoscopic cystograms with the bladder inflated with air. The general condition of the patient must be ascertained with especial emphasis placed upon the cardiovascular and renal reserve.

A bladder cancer should never be treated with fulguration. The electric spark lacks power to destroy fully established cancer, and clinical evidence suggests that such irritating treatments stimulate the tumor to a more rapid growth.

If the size and position of a papillary carcinoma are such that all of the base can be visualized accurately through the cystoscope (approximately 1.5 centimeter in diameter), the tumor may be treated successfully with interstitial irradiation by means of gold seeds inserted through the urethra.[1] When all of the base cannot be seen clearly through the cystoscope, suprapubic cystostomy should be performed and gold seeds embedded under direct, unobscured vision.

Flat, infiltrating bladder carcinomata, irrespective of size, should be treated with radium through the open bladder. The submucous extensions of this disease cannot be detected with sufficient accuracy by cystoscopic vision.

In performing suprapubic cystostomy for radon implantation certain details should be observed. Spinal anæsthesia is recommended. Before opening the bladder, the exposed layers of the abdominal wall are carefully protected with gauze to prevent tumor implants, should any of the bladder contents be spilled. All manipulations are gentle. The bladder is never separated from its attachments, because we think this procedure of mobilization favors dissemination of cancer through lymphatics. Resection is never done. To facilitate burying gold seeds in the base of a papillary tumor, the bulk of the intravesical projection is removed with the actual cautery or endotherm knife. We do not coagulate the base. After the base of the tumor has been exposed clearly, gold radon seeds of 2.0 millicuries each are buried throughout and to a distance of at least 1 centimeter beyond any visible or palpable evidence of involvement. The seeds are buried with precision 1 centimeter apart and 1 centimeter deep so that each seed marks the vertex of an equilateral triangle, the sides of which are 1 centimeter in length.

Flat bladder cancers are treated in the same way except that there is no projecting tumor to remove. We carry out gold seed implantation regardless of the relationship between the tumor and the ureteral orifices. In only 2 cases has operation been necessary to relieve a blocked ureter.

From this description it may be observed that the number of millicuries of radon needed to treat any given bladder cancer depends entirely on the size of the growth. In several instances we have used more than 50 seeds aggregating over 100 millicuries without causing harmful results. We believe that the greatest danger of radiation therapy is the danger of inadequate dosage. Therefore, if an ample supply of radium is not available some other method of treatment should be employed.

After treatment we keep the patient under close observation. Examinations are performed with such frequency that recurrences may be detected while they are small enough to be treated by endoscopic measures. Unfortunately, the appearance of recurrences practically always means that the growth has progressed beyond control. For this reason it must be emphasized that in treating bladder cancers with radium, the urologist must work with the purpose of curing the patient by the first operation. Therefore irradiation must be adequate and thorough.

Any intelligent discussion of the effect of radiation must be based on an estimate of the quantity actually concerned in producing the phenomenon. In the case of regression of a tumor mass, if we

[1] Gold radon seeds of 2.0 millicuries each, buried to the depth of 1 centimeter and 1 centimeter apart have given satisfactory results. If spinal anæsthesia is used, and epinephrin is added to the irrigating solution to prevent bleeding from the needle pricks, the operation may be performed at one sitting. Otherwise the procedure must be repeated until the base of the tumor and an outlying zone 1 centimeter in width have been covered accurately. If the implantation has not been completed within 3 weeks, it sometimes happens that vision will be obscured by slough produced by earlier treatments.

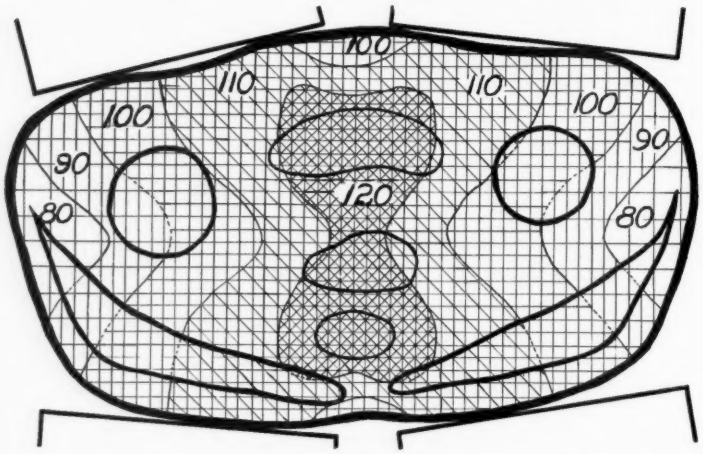


Fig. 1. Cross section of pelvis showing irradiation of the bladder by high voltage roentgen-rays through four skin portals.

consider the effect a direct one on malignant tissue, it is essential to know the amount of radiation arriving at the growth. It is obvious that all points of an irradiated mass cannot receive the same amount of energy; this is particularly true when interstitial radiation is employed. If tumor regression depends on every point receiving *at least* a certain definite amount, then it is necessary to know the quantity delivered at the point which receives the minimum. It is evident that for external radiation a knowledge of the amount leaving the source or falling on the skin is of little value because the amount delivered at a point within the body varies enormously with the depth below the skin. In the case of interstitial radiation, a knowledge of the amount used is not sufficient. We must also know the size and shape of the mass, the distribution of the sources, and the manner in which the effect varies with the distances from the sources.

For convenience we may call the amount of radiation delivered at a given point in the tissue the tissue dose at that point. It is necessary then to have a unit of quantity of radiation in terms of which these doses may be expressed. At the Memorial Hospital, this unit is the threshold erythema dose. This is defined as the amount of radiation which, after a single application, will produce in 80 per cent of all cases a faint bronzing or reddening of the skin in about 3 weeks, and in the other 20 per cent will produce no visible effect. Arguments for the use of this unit have been published previously (1 and 5). The threshold erythema doses for the sources of radium and the roentgen-rays in use at the hospital have been determined by skin tests on a large number of patients. By means of physical experiments, the percentage of the amount of radiation falling on the skin which arrives at any depth within the tissue has been determined. For the treatment of bladder tumors the external sources used are the high voltage roentgen-rays and the radium element pack. Table I shows the percentage of surface radiation arriving at various depths for these applicators.

From this table, if we know the amount of radiation falling on the skin at each portal, in terms of the threshold erythema (S.E.D.), and if we know the depth of the tumor below each portal, we can determine at once the tissue dose from external radiation. Figure 1 represents a cross section of a pelvis, showing the irradiation of the bladder of a medium sized individual by high voltage roentgen-rays through four skin portals. It is seen that the total tissue dose throughout the bladder region is about 1.2 erythema doses—120 per cent threshold erythema.

For interstitial radiation the problem is not so simple. The interstitial sources used in the treatment of bladder tumors at Memorial Hospital are gold seeds about 4 millimeters long, 0.3 millimeter wall thickness, and of about 2 millicurie radon content. Work previously published makes possible the determination of the percentage of a threshold erythema dose delivered at any distance from any gold seed (6 and 7). The values for a seed of 2 millicuries at different distances are shown in Table II.

TABLE I.—DEPTH DOSES FROM HIGH VOLTAGE ROENTGEN-RAYS AND RADIUM ELEMENT PACK

Depth	ROENTGEN-RAYS	RADIUM ELEMENT PACK	
CM.	200 kilovolts 50 cm. T-S Dist. 0.5 mm. Cu. and 2.5 mm. Al. filter 100 sq. cm. field	0.3 mm. Pt. and 1.5 mm. brass filter 50 sq. cm. radiating surface	
		10 cm. distance	15 cm. distance
0	100	100	100
1	99	81	86
3	85	59	67
5	67	44	53
7	52	33	43
10	33	23	31
12	25	18	19
15	17	13	14

T-S, target-skin distance; Cu., copper; Al., aluminum; Pt., platinum.

TABLE II.—TISSUE DOSES FROM A TWO MILLICURIE GOLD RADON SEED AT DIFFERENT DISTANCES

Distance	Tissue dose	Distance	Tissue dose
Cm.	Per cent S.E.D.[1]	Cm.	Per cent S.E.D.
0.5	950	2.25	50
0.6	700	2.5	45
0.7	465	2.75	40
0.8	350	3.0	35
0.9	275	3.5	30
1.0	230	4.0	25
1.2	140	4.5	20
1.4	110	5.0	15
1.6	90		
1.8	75		
2.0	70		

[1] Threshold erythema dose.

With the aid of this table, if we had a chart of any bladder tumor, with the locations and strengths of the seeds which had been implanted, we could measure all their distances from any selected point, and find the total tissue dose at that point due to the individual seeds. If a seed were greater or less than 2 millicuries, the corresponding tissue dose would be proportionately greater or less.

It is impracticable to do this in actual cases. However, it is comparatively simple to represent diagrammatically the various shapes and sizes of tumor masses that might be expected to occur. These growths are so flat and thin that we may consider all the seeds to lie in a single plane. As has already been stated, our usual method of using gold seeds in bladder tumors 2 centimeters or more in diameter, is to expose the growth surgically and implant seeds of approximately 2 millicuries each, spaced 1 centimeter apart at the vertices of equilateral triangles, throughout the mass, and to a distance of 1 centimeter beyond it on all sides. Accordingly, diagrams of a number of possible lesions were made on centimeter cross section paper, the distribution of seeds indicated thereon, the distances from each seed to selected points measured, and the individual tissue doses determined. Three points were used for each diagram: two in the plane of the seeds, which is supposed to be the plane of the base of the tumor, and one on the exposed surface of the growth. Point *1* in each case is at the periphery of the actual mass, in the plane of the seeds; point *2* is 1 centimeter farther out, at the edge of the area in which seeds were implanted; point *3* is directly above point *1*, on the exposed surface of tissue. The same dose would, of course, be received at a similar distance below the plane of the seeds. Figure *2* shows this scheme diagrammatically. The first point gives the minimum dose for the tumor base; the third gives the minimum dose for the surface of the growth; the second indicates our factor of safety for possible infiltrations of tumor cells which are not clinically demonstrable.

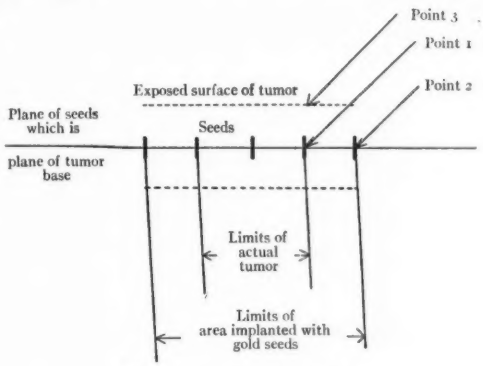


Fig. 2. Implantation of seeds.

Table IIIA shows the diagrams and calculations for points *1* and *2* for circular masses 2 centimeters and 4 centimeters in diameter respectively. Table III gives the complete data for several more of different shapes and sizes, covering the range which might be expected clinically. The first column gives the size and shape of the mass considered, the second, third, fourth, and fifth, the amount of radon used and the tissue doses under our present scheme of treatment: the 4 following the same data for seeds of 1 millicurie instead of 2 millicuries, and the last 4 for a spacing of 1.5 centimeter instead of 1.0 centimeter,

TABLE III.—TISSUE DOSES FROM GOLD SEEDS IN BLADDER TUMORS

Dimensions of mass cm.	2 mc. seeds 1 cm. apart				1 mc. seeds 1 cm. apart				2 mc. seeds 1.5 cm. apart			
	mc.	Skin erythema doses			mc.	Skin erythema doses			mc.	Skin erythema doses		
		Point* 1	Point* 2	Point* 3		Point 1	Point 2	Point 3		Point 1	Point 2	Point 3
2 circle	38	32	24	19	19	16	12	10	22	13	11	9
2.5 circle	46	35	22	20	23	18	11	10	28	14	12	10
3.0 circle	62	35	24	21	31	18	12	10	30	16	11	11
3.5 circle	70	34	22	22	35	17	11	11	34	13	10	10
4.0 circle	74	38	27	25	37	19	14	12	38	14	11	11
4.5 circle	86	35	24	24	43	18	12	12	42	17	12	12
5.0 circle	106	37	27	25	53	19	14	12	54	16	12	12
2x3 ellipse	54	32	23	20	27	16	12	10	28	14	12	10
3x4.5 ellipse	74	37	25	24	37	19	12	12	38	15	12	10
4x6 ellipse	106	36	25	23	53	18	12	12	54	17	13	12
1x3 ellipse	42	34	24	20	21	17	12	10	18	13	10	8
2x5 ellipse	54	35	23	22	27	18	12	11	42	17	12	12
3x7 ellipse	102	35	22	22	51	18	11	11	38	12	9	8

*Points *1* and *2* are in the plane of the centers of the seeds, which is the plane of the base of the tumor. Point *1* is at the edge of the demonstrable lesion, point *2* is 1 centimeter farther out, at the edge of the "seeded" area. Point *3* is on the exposed surface of the tumor, directly over point *1*, and therefore 0.8 centimeter from the plane of the center of the seeds. The same dose as for point *3* would be delivered at a point situated at an equal distance deeper in the tissues. The dose at point 3 is the minimum dose delivered to the tumor.

with seeds of 2 millicuries.[1] It is seen that with our present technique the doses on the exposed surface of the tumor, and at the base of the growth, in the bladder wall, are in the neighborhood of 20 erythema doses (point *3*).

It is evident that these doses must not be interpreted as actual minimum tissue doses in any given cases. Practically there will be variations due to somewhat different spacings as well as variations in the strength of the seeds. However, from them we may draw some interesting conclusions regarding the treatment of bladder tumors by this method. In the first place, for each type of treatment, the minimum dose is practically the same regardless of the size of the mass and the number of tubes used. This is due to the fact that the greater part of the dose is delivered by the few seeds close to the point in question, the more distant ones contributing but little to the total. This is evident from a glance at Table IIIA. Of course, the delivered dosage with 1 millicurie seeds is just half that obtained with the same number of 2 millicurie seeds. It is interesting to note that, with 1.5 centimeter spacing and 2 millicurie seeds, in any given case the number of millicuries used is equal to or greater than that for 1 millicurie seeds and 1 centimeter spacing, yet the tissue dose is less. Evidently in lesions of the configuration of bladder tumors, a large number of relatively weak sources is preferable to fewer stronger ones.

[1] The doses are given to the nearest whole number, the method of deriving them does not warrant the assumption of greater accuracy. Small variations in arranging the seeds, or in the positions of the points selected may cause variations of 2 or 3 threshold erythema doses in the total doses, but such differences are unimportant at present.

The doses which we apply to bladder cancers are large compared to those which have been quoted for any other region of the body. Even the doses 1 centimeter outside the actual lesion are more than double those used in other conditions. In intra-oral squamous carcinoma, regression may be expected to follow the administration of about 10 erythema doses (4). In adenocarcinoma of the breast, doses of the same order of magnitude are used (3). In carcinoma of the cervix uteri, 5 or 6 erythema doses seem to be effective (2).[2] However, since the bladder is a relatively inaccessible organ and each suprapubic implantation requires a major operation, our efforts have been directed toward curing the patient by a single treatment. In addition, our patients do not react so unpleasantly as to require us to modify our dosage. Finally, our own belief is that whatever success has followed our methods has been due largely to the intensity of the radiation we have used.

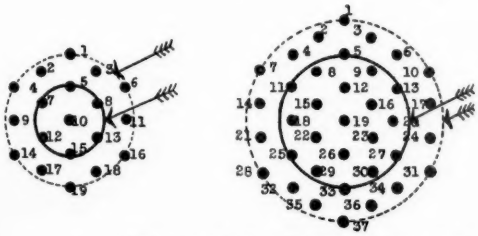
Comparing a not unusual interstitial irradiation of 20 threshold erythemas doses with the maximal 1.2 threshold erythema doses delivered by external sources, it is obvious why roentgen-rays and the radium element pack have proved of so little value in curing bladder cancers. Unquestionably these external sources can furnish useful palliative radiation which may promote absorption of pericystitis and relieve pain, but they cannot be relied upon to effect a cure.

[2] The doses described in this paper are based upon methods which have been developed empirically. Until the present time no calculation has been made of the tissue dose. The data given here show the distribution of radiation from these massive doses. In view of the fact that our applications are so much greater than those which have been found satisfactory in other departments, it is possible that later experience, guided by physical calculations, may favor a lesser dosage.

TABLE IIIA.—DIAGRAMS AND CALCULATIONS FOR POINTS *1* AND *2*[1] FOR CIRCULAR MASSES TWO AND FOUR CENTIMETERS IN DIAMETER RESPECTIVELY

Gold radon seeds—2 mc. each—1 cm. apart. Dose on periphery of tumor, and 1 cm. outside, due to each seed—per cent S.E.D.

2 cm. tumor—10 seeds—38 mc.			4 cm. tumor—37 seeds—74 mc.		
Seed No.	Per cent S.E.D. Periphery	Per cent S.E.D. 1 cm. out	Seed No.	Per cent S.E.D. Periphery	Per cent S.E.D. 1 cm.
1	50	90	1	30	25
2	45	50	2	25	20
3	90	700	3	40	35
4	35	35	4	20	15
5	110	100	5	40	30
6	180	700	6	60	45
7	75	45	7	15	10
8	700	230	8	30	25
9	40	30	9	75	45
10	230	70	10	80	90
11	350	100	11	25	15
12	75	35	12	50	35
13	700	70	13	230	90
14	35	25	14	15	10
15	110	35	15	35	25
16	180	45	16	180	50
17	45	30	17	410	700
18	90	35	18	30	15
19	50	30	19	70	35
Total	3190	2455	20	950	100
			21	15	10
			22	35	25
			23	180	50
			24	410	700
			25	25	15
			26	50	35
			27	230	90
			28	15	10
			29	30	25
			30	75	45
			31	80	90
			32	20	15
			33	40	30
			34	60	45
			35	25	20
			36	40	35
			37	30	25
			Total	3770	2680



[1] Point 1 at edge of tumor, in plane of center of seeds; point 2, one centimeter outside of tumor in same plane.

RESULTS

An accurate computation of end-results following the use of any method of treatment is of value principally in furnishing a basis of comparison with the end-results of other methods. In a study of carcinoma of the bladder, the comparison is between radiation and surgery. Although radiation therapy of bladder cancer is still in a developmental stage, the writers believe that it can be demonstrated that (1) the use of physical agents offers success where operation short of total cystectomy can offer nothing; (2) the use of radiation is attended with a lower primary mortality; and (3) with radiation the tumor is controlled more effectively than with surgery alone.

At the Memorial Hospital, we do not refuse radium implantation to any patient whose cancer is confined to the bladder, or who is not moribund from the effects of prolonged disease. Many of the cancers we treat are so extensive as to involve a third or more of the bladder. In 62 per cent of the patients we have operated upon, cancer touched the ureteral orifices, the trigone, or both. A large proportion of these cases would be considered inoperable from the standpoint of surgery alone. Of course, they would not be included in surgical end-results.

In regard to operative mortality the use of radiation is much to be preferred. In practicing segmental resection, which not infrequently requires ureteral transplantation, the most skillful surgeons have an operative mortality of from 10 to 20 per cent. In 106 consecutive operations with the implantation of gold seeds our operative mortality was 3.7 per cent.

Following Broders' classification of epithelial tumors on the basis of malignancy, certain surgical end-results have been published which include the follow-up record of all four groups. These have included many tumors of group 1, which are benign papillomata. Such figures are not relevant to a study of cancer. It should be clearly understood that no benign tumors are included in this series.

Perhaps some misunderstanding has arisen in the past concerning the use of the term "controlled" as applied to tumors that have been irradiated. Our patients in whom the carcinoma has been controlled present no symptoms nor signs of disease after the most painstaking examination.

TABLE IV.—PAPILLARY CARCINOMA, OR PAPILLOMA WITH ATYPICAL CELLS—DIAGNOSIS MADE BY HISTOLOGICAL, NOT CLINICAL, EXAMINATION

	Cases	Per cent
Number of cases	51	
Controlled	27	52.9
Controlled over 3 years	22	43.0
Not controlled	24	47.1

Summary—Years since treatment	Controlled	Not controlled
Less than year	2	10
1 to 2	2	9
2 to 3	1	1
3 to 4	2	1
4 to 5	3	1
5 to 6	6	1
6 to 7	1	0
7 to 8	3	1
8 to 9	3	0
9 to 10	3	0
10 to 11	1	0

TABLE V.—PAPILLARY CARCINOMA. DIAGNOSIS CLINICAL. PAPILLOMA WITH ATYPICAL CELLS ARE INCLUDED

	Cases	Per cent
Number of cases	45	
Clinical and histological diagnoses agree	36	
Clinical and histological diagnoses disagree	9	
Controlled	30	66
Controlled over 3 years	25	55.5
Not controlled	15	33.0

Summary—Years since treatment	Controlled
Less than year	1
1 to 2	3
2 to 3	0
3 to 4	2
4 to 5	6
5 to 6	3
6 to 7	3
7 to 8	2
8 to 9	2
9 to 10	5
10 to 11	1
11 to 12	0
12 to 13	1

TABLE VI.—INFILTRATING CARCINOMA—DIAGNOSIS MADE BY HISTOLOGICAL, NOT CLINICAL, EXAMINATION

	Cases	Per cent
Number of cases	44	43.1
Controlled	19	43.1
Controlled over 3 years	14	31.8
Not controlled	25	56.9

Summary—Years since treatment	Controlled	Not controlled
Less than year	2	12
1 to 2	2	7
2 to 3	1	2
3 to 4	2	1
4 to 5	2	1
5 to 6	2	1
6 to 7	2	0
7 to 8	2	0
8 to 9	0	0
9 to 10	3	1
10 to 11	0	0
11 to 12	0	0
12 to 13	0	0
13 to 14	1	0

TABLE VII.—INFILTRATING CARCINOMA—DIAGNOSIS CLINICAL

	Cases	Per cent
Number of cases	82	
Clinical and histological diagnoses agree	44	
Clinical and histological diagnoses disagree	38	
Controlled	30	36.5
Controlled over 3 years	23	27.8
Not controlled	52	63.5

Summary—Years since treatment	Controlled
Less than year	3
1 to 2	2
2 to 3	2
3 to 4	4
4 to 5	3
5 to 6	3
6 to 7	4
7 to 8	3
8 to 9	2
9 to 10	3
10 to 11	0
11 to 12	0
12 to 13	0
13 to 14	1

We do not use the word "cured," because we do not as yet know all of the criteria of ultimate success in the treatment of bladder cancers.

The results obtained from radiation applied to papillary carcinomata are indicated in Tables IV and V. Not infrequently there is a difference of opinion between the clinician and the pathologist regarding the exact nature of a tumor. Compared with the histological diagnosis, clinical observations are not to be despised, especially in those cases in which only a small fragment from a superficial part of the tumor has been submitted to the pathologist. In order to prevent any question arising as to the standards by which the tumors were diagnosed, separate classifications are presented.

The tumors of Table IV were diagnosed purely by histological criteria. Their general structure was papillary but atypical or cancerous cells were present. Of the 51 cases comprising this group, 27, or 52.9 per cent, have been controlled to date. Twenty-two, or 43 per cent, of the entire group have remained free from disease for from 3 to 10½ years after irradiation. Forty-seven per cent were

not controlled, although 4 patients lived from 3 to 8 years after irradiation. The fact that approximately 80 per cent of the uncontrolled patients died within 2 years of treatment indicates a large field for improvement. In general these were the most advanced cases; many were recurrences after operation. Probably we can better these results by modifying our methods, but radical improvement will come only when earlier diagnoses are made and when the initial treatment is more effective.

In Table V, the tumors are classified on the basis of clinical examination. Solid, club-shaped, sessile tumors, often multiple, when partly or wholly covered with slough, were diagnosed papillary carcinoma. Of this group of 45 cases, 25, or 55.5 per cent, have been controlled for from 3 to 13 years.

The discrepancies between the clinical and histological diagnoses in Tables IV and V are accounted for partly because a few cases of clinical cancer were diagnosed in the laboratory as papilloma, and a number were considered to show histological evidence of infiltrating the bladder wall. In the majority of cases the diagnosis is the same by each standard.

Tables VI and VII indicate the results with infiltrating cancers. The histological evidence of this type of tumor consisted in the presence of cancer cells invading the structures of the bladder wall. Marked induration of the base of the tumor was considered positive clinical evidence of infiltration. This feature was detected by digital palpation or was demonstrated when radium needles encountered tumor tissue of the density of leather. Frequently infiltration of the bladder wall by tumor was shown in the cystograms, but such findings were not made the basis for a positive diagnosis.

In comparing Tables VI and VII it will be noted that all of the tumors diagnosed as infiltrating by histological examination were found to have clinical features of infiltration as well, but a large number of tumors were classified as infiltrating on the basis of clinical observation when the microscopic findings could not detect invasion of the bladder wall. It is likely that in these cases the biopsy specimens did not contain sufficient tissue from the base of the tumors. That there was probably no great discrepancy between the characters of these tumors whether diagnosed by histological or clinical methods is shown in the results after treatment. In each group the patients controlled for more than 3 years after radiation comprised approximately 30 per cent of those treated.

SUMMARY

If the base of a papillary carcinoma is no larger than 1.5 centimeter in diameter and is entirely visible through the cystoscope, the tumor may be treated successfully with gold radon seeds implanted through the urethra. Larger papillary cancers and all infiltrating tumors should be treated under full vision with the bladder opened.

The operation of suprapubic cystostomy with implantation of radon seeds requires painstaking technique, the most important features of which are protection of the wound against tumor implants, great gentleness, never mobilizing the bladder, accurate radon implantation, and an adequate number of gold seeds of proper strength.

Careful estimates show that 1.2 threshold erythema doses is about as large a dose as can reach a bladder tumor from a single pelvic cycle of 4 high voltage roentgen-ray treatments.

A table is presented which indicates the tissue dose of radiation delivered at various distances from a 2 millicurie gold seed. With the aid of this table and diagrams representing cross sections of the base of bladder tumors, the minimum tissue dose that we use in treating bladder cancers was found to be between 20 and 25 threshold erythema doses. A centimeter beyond all demonstrable tumor the tissues receive from 20 to 30 threshold erythema doses. We believe that this is an important factor of safety in view of the great difficulty in estimating accurately the extent of an infiltrating tumor. These figures indicate the greater intensity of interstitial radiation and perhaps explain the failure of many attempts to cure bladder tumors with treatment derived from external sources.

We use relatively large doses of interstitial radiation because it is essential that malignant tumors in an organ as inaccessible as the bladder should be cured by a single treatment.

Our results indicate that with the use of adequate doses of interstitial radiation:

1. We can offer hope of cure to patients to whom operation alone, short of total cystectomy, can offer nothing.

2. Our operative mortality is less than that from surgery alone in the proportion of 3.7 per cent compared with 10 to 20 per cent.

3. In a series of papillary bladder cancers, between 43 and 55 per cent of the patients are free from symptoms and signs of disease 3 years after treatment.

4. In a series of infiltrating bladder cancers, between 27.8 and 31.8 per cent of the patients are free from symptoms or signs of disease 3 years after treatment.

From our experience with radium therapy as it is employed at the Memorial Hospital we believe that an adequate dose of interstitial radiation is preferable to surgery alone in the treatment of both papillary and infiltrating types of bladder cancer because after radium implantation the operative mortality is less and a higher percentage of patients are found free from disease 3 years after treatment.

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URINARY INCONTINENCE FOLLOWING CHILDBIRTH; ITS SURGICAL TREATMENT

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A GREAT deal has been written on incontinence of urine in the female, and many and varied have been the operations to relieve it. It is of common occurrence, a very distressing symptom, and often made light of—the women taking it as a natural sequel to childbirth and resigning themselves to this annoying condition.

Taylor and Watt, reviewing the records of 1,006 gynecological cases in the Roosevelt Hospital, found incontinence in 15 per cent, and the percentage increased with the number of children the patients had borne.

That incontinence of urine is always associated with cystocele, prolapse of the vault or uterus is incorrect. Very often the reverse is true, a bad procidentia having complete control.

It depends upon the displacement of the upper part of the urethra; that part which is held in position by the triangular ligament and surrounded by the sphincter urethræ or compressor urethra. As long as the sphincter urethræ muscle remains intact the control is good. This muscle supports the upper part of the urethra and when it is torn allows a sagging of this part, so that when the patient coughs or sneezes the urethra becomes displaced; the meatus looking upward and forward, and the urine being expelled in a spurt.

THE ANATOMY OF THE FEMALE URETHRA AND ITS ATTACHMENTS

The base of the bladder rests upon, and is supported by, the deep layer of the triangular ligament and a musculofascial sheet, the so called pubocervical layer of pelvic fascia which separates it from the anterior vaginal wall. Tearing of this musculofascial sheet allows a herniation of the bladder to occur—a cystocele. The triangular ligament is perforated anteriorly by the urethra and the part of the urethra lying between the two layers of the ligament is surrounded by a striped muscle of goodly size—the sphincter urethræ. It is the voluntary muscle of micturition. The sphincter embraces the urethra. The component fiber bundles arise from the fibrous tissue in the angle beneath the symphysis pubis and from the descending pubic rami. They pass analward and medialward on each side of the urethra, interdigitating across the median line, and joining their fellows of the opposite side (Fig. 1).

The fibers, posteriorly as well, terminate in the anterior vaginal wall, to which they are firmly attached (Fig. 2).

The anterior group of fibers are well protected and are rarely torn (Fig. 3). The posterior and sling group of fibers lying between the urethra and the vaginal wall are easily torn by the advancing head, as it forces the vaginal wall downward in its descent and tears the muscle bundles that are attached thereto. If the pressure is severe and prolonged, those bundles interdigitating across the midline are also damaged.

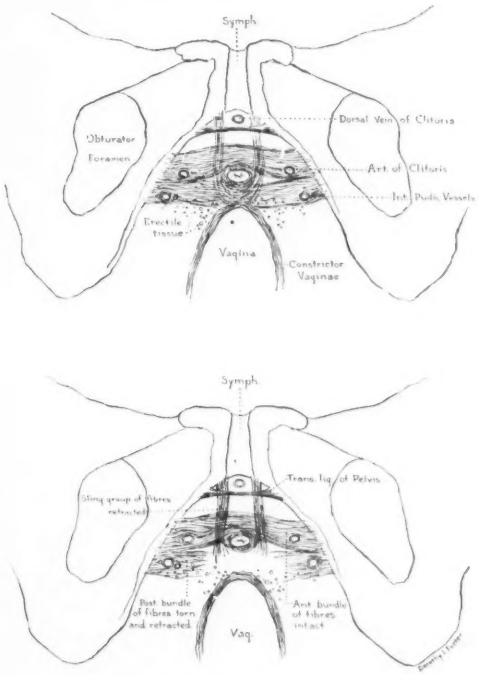

Fig. 1. Diagram showing the three groups of muscle bundles composing the sphincter urethræ muscle and their relation to the urethra and the anterior vaginal wall. The lower part of the diagram shows the posterior and sling group of bundles torn and their retraction upward and outward.

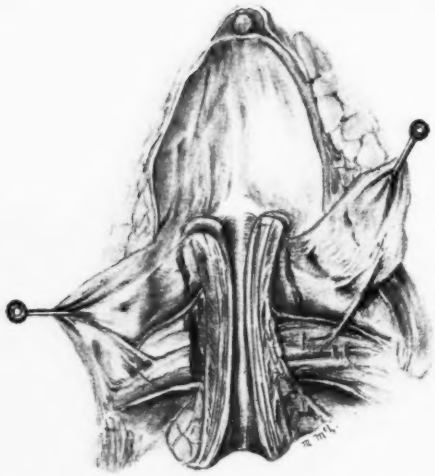

Fig. 2. Drawing made from a dissection by the author (autopsy specimen) of a patient who had never borne children. The urethra is laid open along its posterior wall and the vaginal walls are reflected laterally. One can see the vestibule, clitoris, labia minora, meatus urinarius, the two layers of the trigone, and the sphincter urethræ muscle (posterior group of fibers) lying between the two layers of the ligament. Deep to the ligament can be seen the sphincter vesicæ. The urethral sphincter fibers are attached to the anterior vaginal wall and are dissected away with difficulty.

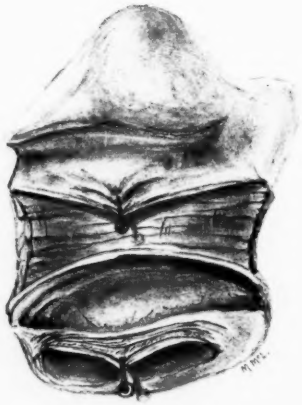

Fig. 3. This is a dissection of the urethra under the symphysis pubis. One can see the two layers of the trigone with the sphincter urethræ muscle (anterior group of muscle fibers in between the two layers). The bladder neck is being held back from the trigone by a hook. The other hook is drawing the superficial layer of the trigone over the sphincter urethræ muscle.

The torn muscle now retracts and the intervening space is filled in by scar tissue, so the efficiency of the sphincter is weakened (Figs. 1 and 4). Microscopic and macroscopic examinations of the internal or vesical sphincter show it to be a small muscle. It is the thickened circular group of muscle fibers around the neck of the bladder, is involuntary in its action, and being part of the viscus, descends with it unhurt in childbirth (Figs. 2, 3, and 4). Bonney in his paper on diurnal incontinence, describes the structures surrounding the urethra as the peri-urethral wedge. This I take to be the internal sphincter, the two layers of the triangular ligament, and the structures lying between the two layers of the ligament. He considers the sphincter to play only a small part in urinary control, and he is inclined to think that control is helped by tightening the anterior end of the pubocervical muscle sheet.

That the sphincter urethræ is the important factor in maintaining control is borne out by the fact that control is good when it is intact and poor or lost when it is not. There is no doubt that tightening the anterior end of the pubocervical sheet should help it, as some fibers of the sphincter urethræ spread themselves out on the vaginal wall, but the bulk of the muscle shrinks outward and upward when it is torn, and so should be located and the torn ends approximated, if good control is desired. I do not mean to imply that the supporting structures are of no importance. On the contrary, the stronger and tauter they are, the firmer the *point d'appui* for the sphincter and the more efficient its action. So also if a cystocele exists it should be repaired by drawing across the torn sides of the pubocervical sheet which extends from the symphysis pubis to the cervix, and on which the bladder rests. By repairing the supporting mechanism the bladder is again in its normal anatomical position—the frequency of micturition is helped, and a firm base formed for the sphincter. The cystocele is repaired by the method suggested by Professor Watson in the *British Medical Journal* of September, 1924.

TREATMENT

I shall briefly review a few of the operations that have been performed.

1. Insertion of a pessary. This is a useless precedure, as it does not help to relieve the anatomical defect which is the cause of the disturbance.

Fig. 4. This is a dissected specimen of a woman who died in the Medical Wards of the Toronto General Hospital, from pulmonary tuberculosis. She had had a difficult childbirth 7 years before and had suffered from incontinence of urine. The probe is in the urethra, the end lying just below the clitoris. The anterior vaginal wall has been medially incised and one side dissected, showing the torn end of the sphincter urethræ muscle, lying just below the deep layer of the trigone, and retracted outward. One can also see the sphincter vesicæ surrounding the neck of the bladder.

Fig. 5. Gentle traction on the catheter reveals the neck of the bladder. The line marks the incision.

2. Frank's operation. Excision of a wedge shaped piece of tissue from the vaginal and urethral walls.

3. Dudley's operation. Advancement of the urethra. The urinary meatus is displaced and is brought to lie beneath the clitoris, giving the urethra a sharp angle.

4. Gersuny's operation. Torsion of the urethra.

5. Gersuny-Pawlik-Ries operation. Torsion of the urethra with advancement and tunneling.

6. Kelly's operation. Mattress suturing of the vesical neck and the sphincter vesicæ with silk.

May I venture to suggest that this very able and world-famed gynecologist secured his results by possibly picking up some of the fibers of the sphincter urethræ in suturing the internal sphincter?

I believe the great majority of patients suffering from incontinence of urine following childbirth can be cured by apposing the torn ends of the sphincter urethræ muscle. The patient is placed in the lithotomy position and a Pezzer or mushroom catheter is introduced into the bladder. Gentle traction on the catheter reveals the neck of the bladder (Fig. 5).

The anterior vaginal wall is now medially incised from a little above the urethro vesical junction down toward the meatus and the vaginal flaps are reflected laterally.

The thickened neck of the bladder can now be felt. Directly below and stretching from side to side can be seen the deep layer of the trigone which is pearly white in color. By careful dissection far out on the sides just below this layer, the torn ends of the sphincter can be isolated, freed, and an Allis forceps applied to each end (see Figure 6, 2—in the diagram the Allis forceps is omitted). The catheter is now withdrawn. These muscle ends are usually far out and pulled upward

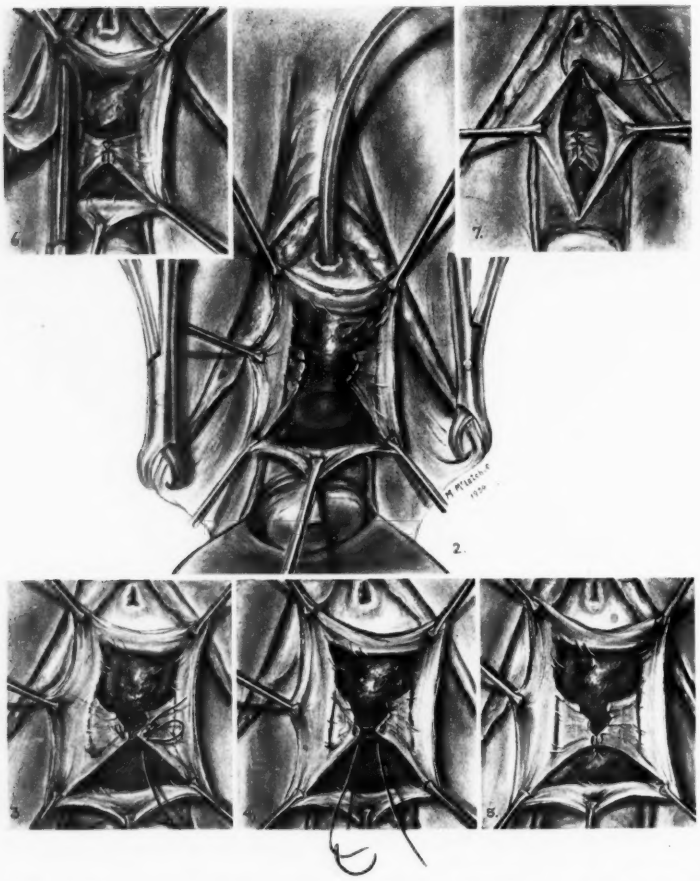

Fig. 6. The torn ends of the sphincter urethræ muscle isolated; *3* and *4* show stitch picking up the deep layer of the trigone and the torn muscle ends; *5* tying the first stitch; *6* completing the approximation and excising the redundant vaginal mucosa; *7* sewing up the vaginal mucosa.

and outward, an action which can be easily understood as the posterior and sling group of muscle fibers have been torn. The sphincter urethræ muscle has no sheath; the sheath of this muscle and that of the deep transversus peronei, having become differentiated out to form the two layers of the trigone, so that in the majority of these cases the deep layer is relaxed or partially torn.

Advantage is taken of this to include as well in my first stitch the deep layer of the trigone. This tough membrane helps to hold the muscle ends in place, and prevents tearing out of the stitches until healing is complete (Fig. 6, *3, 4, and 5*). Two or three more interrupted stitches complete the approximation *6*. The material used is chromic gut No. 0 on a small round needle.

The next step is the excision of the redundant vaginal mucosa (Fig. 6, *6*). This obliterates the dead space, helps to support the urethra, and tends toward better healing (Fig. 6, *7*). The vaginal mucosa contains a few muscle fibers from the sphincter, and so is part of the sphincteric mechanism.

One of the difficulties encountered is bleeding. The hæmorrhage is always troublesome from the numerous erectile tissue spaces found around the urethra. Sometimes the artery to the clitoris or one of its branches is wounded. Free bleeding ensues which is very difficult to control as the vessel retracts far out into the trigone and is hard to find. It is most important to leave the field dry as bleeding prevents healing and makes a good harbor for infection.

A permanent catheter is now introduced. A four winged catheter with the two holding straps inside the wings removed works very well. This type of catheter collapses easily during its withdrawal and does not tear out the stitches in the muscle. It is removed in 4 days' time (Fig. 7).

The patient is given 5 grains urotropin thrice daily and nursed in a semi-sitting position on a Gatch bed.

Of the 6 cases operated upon by this method in private and in the gynecological wards of the Toronto General Hospital, there have been 5 cures. The other case failed on account of premature separation of the stitches due to an infected hæmatoma. These cases have been observed for 3 to 12 months.

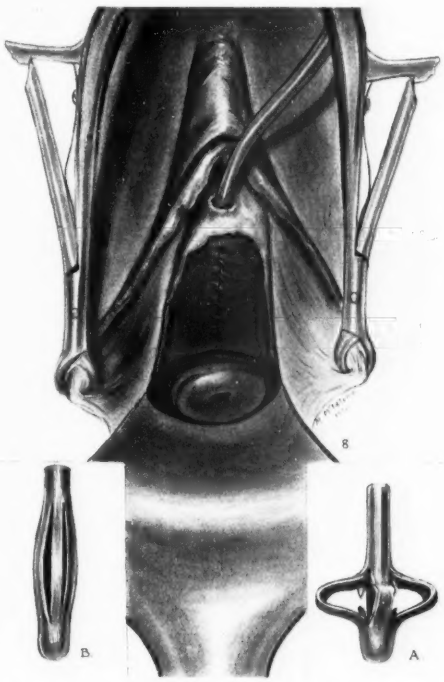

Fig. 7. Retention catheter in place. Views *A* and *B*, show type of catheter used.

I am indebted to Professor Hendry of the department of obstetrics and gynecology and to Professor J. C. Watt of the anatomy department for their help and enthusiasm in the work and to Miss McClatchie and Miss Foster, artists of no mean ability. I hope that this operation may be of some use in helping those women whose lives have been made miserable as the result of childbirth.

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HYPERNEPHROMA: EXTENSION TO THE URETER[1]

FREDERICK W. SCHACHT, M.D., WINNETKA, ILLINOIS

THE case reported here is that of a rather unusual type of hypernephroma of the left kidney in which the growth extended into the wall of the ureter.

A man, aged 55 years, came to The Mayo Clinic February 9, 1927, complaining of "kidney trouble." He had been operated on elsewhere for right hydrocele, in 1923. One year before admission to the clinic he had been struck in the lower part of the abdomen as he fell while on a train. When he reached home he began to pass blood from the bladder. Three days after the injury he had three severe attacks of pain in the left lower quadrant. Symptoms were absent after the third attack until hæmaturia reappeared 6 months later. During the first week in February, 1927, he was forced to leave work because of pain in the lower part of the abdomen and inability to urinate. The following day a cystoscopic examination was made and the patient was told he had a tumor. There was some burning on urination but no undue frequency.

The patient was anæmic and had lost 39 pounds during the last year. Pupils reacted to light slowly. Tumor was palpated in the abdomen. The left lobe of the prostate gland was more prominent than the right. The systolic blood pressure was 100 and the diastolic 70 millimeters of mercury. The pulse rate was 66 a minute. The urine appeared normal except for erythrocytes graded 1 and pus graded 3. The hæmoglobin was 53 per cent, erythrocytes numbered 4,640,000, and leucocytes 6,600. The color index was 0.5+. The blood urea was 25 milligrams in each 100 cubic centimeters; the Wassermann reaction of the blood was negative. The intravenous phenolsulphonephthalein test yielded 45 per cent.

Fig. 1. Cut surface of the kidney showing involvement of the upper pole by the hypernephroma (half size). Demarcation of the tumor from the renal parenchyma by its encapsulation may be noted.

Roentgenograms of the kidney, ureter and bladder, and lungs were negative. A pyelogram of the left kidney revealed the pelvis to be normal and lying horizontally. The upper and middle calices were elongated, with a large area devoid of medium between; the lower calix was practically normal, and the kidney was somewhat ptosed. The differential phenolsulphonephthalein test was 15 per cent on the right side and 4 per cent on the left. A diagnosis of hypernephroma of the upper pole of the left kidney was then made.

Nephrectomy was performed and a hæmorrhagic degenerating hypernephroma with extension into the pelvis was found. The specimen weighed 610 grams and measured 10 by 7 by 8 centimeters. Seventy-five per cent of the renal substance had been destroyed (Figs. 1 and 2).

The patient's recovery was uneventful. He received a series of deep roentgen-ray treatments and was dismissed from observation March 13, 1927. He returned to the clinic January 3, 1928. One week previously he had had a severe attack of pain in the left side radiating to the testis, and of hæmaturia since the onset of the attack. The patient had regained 29 pounds in weight. The ureterogram of the left side at this time demonstrated that the ureter was not filled; about 1 centimeter of the upper part was evidently considerably dilated (Fig. 3).

Cystoscopic examination at the time did not reveal bleeding, although a few small clots were found in the bladder. The surface surrounding the left meatus was reddened for 1 centimeter. Considerable blood followed the passage of a catheter in the left ureter and a few small fragments were withdrawn from its upper end with a syringe. These fragments were found to be inflammatory degenerating tissue. In view of the cystoscopic and ureterographic data, it was thought advisable to remove the ureter.

Partial ureterectomy was performed extraperitoneally. A lateral muscle-splitting incision was made 3.75 centimeters inside the anterior superior spine of the left ilium. The ureter was located and a small tumor was found in the upper end, 1.25 centimeters below the point sectioned when nephrectomy was performed. The upper end of the ureter was stiff and thick; the lower end in the pelvis was normal. The ureter was ligated 2.5 centimeters below the brim of the pelvis and sectioned.

The pathologist found a hæmorrhagic hypernephroma in the wall of the ureter. The ureter was 10.5 centimeters long, the upper 2.5 centimeters of which was involved in the recurrence. At the inferior border of the tumor a hæmorrhagic papillomatous hypernephroma (2 by 1 centimeter) was found attached to the wall of the ureter (Figs. 4, 5, 6, and 7).

The patient's recovery was rapid and uneventful. He was dismissed from observation January 24, 1928.

REVIEW OF CASES

Kelly, in 1898, reported a case of hypernephroma of the right kidney in which a plug of newgrowth projected into the pelvis of the kidney; ureteral involvement was not mentioned. Albarran and Imbart, in 1903, reviewed 83 cases of hypernephroma but did not mention extension into the ureter. They also reviewed 53 cases of

[1] Work done in the Section on Surgical Pathology, The Mayo Clinic, while a fellow in Urology, The Mayo Foundation, Rochester, Minnesota.

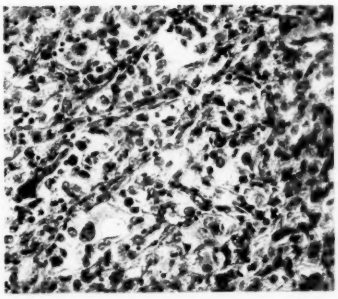

Fig. 2. The characteristic structure of hypernephroma such as fibrous core arrangement and fat vacuoles (x150).

Fig. 3. Filling defect in upper portion of the left ureter.

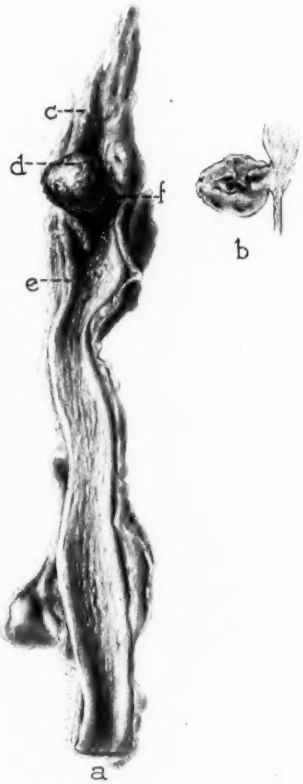

Fig. 4. Specimen removed January 9, 1928, 11 months after nephrectomy; *c* tumor, *d* papilloma, *a* to *e* normal ureter; *b* semidiaphragmatic midsaggital section showing the papilloma arising at the margin of the tumor with the normal ureter below.

tumors in the pelvis of the kidney and ureter without finding this type of tumor.

Shattuck, in 1906, reported a case in which the tumor extended half the length of the ureter. This, he stated, proved to be a typical hypernephroma. He did not state, however, whether the tumor involved the wall of the ureter. Garceau, in 1909, reviewed 176 cases of hypernephroma (with clinical evidence only in most cases) and found 2 which he thought had involved the ureter. A report by Bissell, in 1913, stated that he encountered unmistakable hypernephroma of the left kidney which extended into the pelvis of the kidney and down the ureter. The tumor also

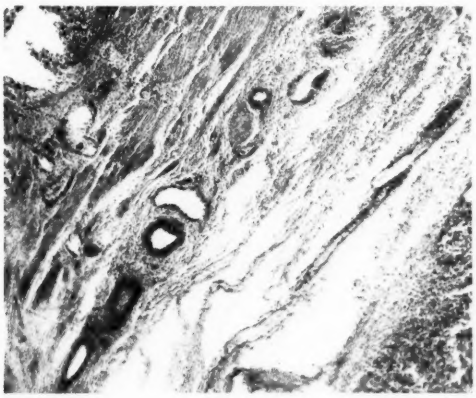

Fig. 5. Section through *c* of Figure 4 showing the involvement of epithelial lining and submucosa by hypernephroma and the replacement of the muscularis by fibrous tissue. Adjacent to the tunica adventitia the tumor may be noted (x40).

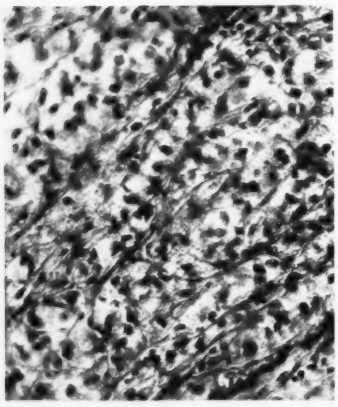

Fig. 6. Section through *c* of Figure 4. This photomicrograph shows the characteristic structure of hypernephroma (x150).

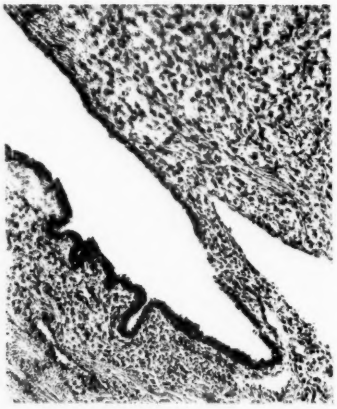

Fig. 7. Section from *f* of Figure 4. The upper portion illustrates tumor involving one side of the ureter completely, with exception of the epithelial lining (x75).

extended into the mouth of the left renal vein. He noted that the muscularis was replaced by fibrous tissue and thought it highly probable that extension took place along the mucosa and submucosa.

A review of the 285 cases of hypernephorma seen at The Mayo Clinic from 1910 to 1928 disclosed 2 cases in which this type of tumor extended into the ureter. The case reported here was the only one in which there was definite involvement of the wall of the ureter. In the other case the tumor projected into the pelvis and lumen of the ureter, but histologic examination did not disclose invasion of the wall of the ureter. Extension into the pelvis of the kidney and the renal veins occurred more often. Many extensive invasions of the renal veins and vena cava have been reported by MacCallum, Oberndorfer, Keyser and Foulds, and others.

Thomas and Regnier, in 1924, reviewed 248 cases of tumor of the renal pelvis and ureter in which hypernephroma was observed. Papillary epithelioma of the pelvis of the kidney, on the other hand, is often implanted in the ureter or bladder.

So far as I have been able to learn from the literature, the case presented here and the one reported by Bissell are the only cases in which there is definite evidence of involvement of the wall of the ureter by the hypernephroma.

Such tumors are usually disseminated by metastasis through the blood stream, rarely by way of the lymphatics, by implantation into the peritoneal surface, or by direct extension to adjacent tissue, as in one case observed in The Mayo Clinic series in which metastatic tissue was found in the perirenal fat. It seems probable that in the case reported here a tuft of the hypernephroma was implanted on the ureteral mucosa, as the line of section at the time of the nephrectomy did not show evidence of involvement.

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THE TECHNIQUE OF SECONDARY OPERATIONS FOR HYPERTHYROIDISM

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The Lahey Clinic

IN our experience with hyperthyroidism of all types, it has been repeatedly impressed upon us that in the presence of true hyperthyroidism the removal of an adequate amount of hyperplastic tissue from the neck will result in a cure of the disease. Failure to cure supposed hyperthyroidism by surgery is due to one of two things: first, the diagnosis of hyperthyroidism as originally made was incorrect, or, second, if the diagnosis was correct the surgery was either incomplete or inadequate.

In a study which was made of recurrent hyperthyroidism some years ago,[1] it was pointed out that two types of hyperthyroidism may occur after thyroidectomy for hyperthyroidism. The first, and relatively more common type, is what we termed "persistent hyperthyroidism." In this disease we are faced with the fact that the patient has never been cured by the original surgery. Although the metabolism comes nearly to normal for a short time after operation and there is some clinical improvement, it nevertheless soon rises again to a position which is nearly as high, or even higher, than that preceding the original surgery and the clinical improvement rapidly disappears. In this type of patient the hyperthyroidism may truly be said to be "persistent." In other words, it has never been cured by the removal of sufficient thyroid tissue. In the second type of patient, however, a condition exists which we term "recurrent hyperthyroidism." It is apparent from the study of the metabolism records of such a patient over many months or even years that an apparent cure of the disease had occurred after the primary operation. The symptoms have been absent and the metabolism normal for a long period of time, such as a year or more, when due to some unknown cause all the symptoms of the disease return and a true recurrence of the hyperthyroidism is discovered.

In any thyroid clinic in which careful postoperative examinations are made, there will be found patients who present either persisting hyperthyroidism or recurrent hyperthyroidism, and it is necessary to develop some definite plan of treatment for these cases. For some time it has been our custom to try Lugol's solution first in all these patients. In very rare instances this will be all that is necessary to control toxicity. There are, apparently, certain rare instances in which, following thyroidectomy for hyperthyroidism, the patients present many symptoms of thyroid intoxication which are controlled completely by the daily administration of 10 drops of Lugol's solution. It is to be emphasized, however, that this type of case is extremely rare and that toxicity after operation is seldom permanently controlled by Lugol's solution. In these patients, we consider that a period of 6 months is adequate to determine whether the postoperative toxicity is entirely controlled by Lugol's solution or whether there is a marked hyperthyroidism which demands further surgery for its cure. We do not feel that a patient is "cured" of hyperthyroidism when there are any clinical or metabolic evidences of toxicity, and we believe that the presence of definite toxicity is sufficient reason for further thyroid surgery.

Since it will be necessary to remove further thyroid tissue from patients who have had a previous thyroidectomy it becomes essential that we establish some definite routine and technique of operation which we may follow to obtain the desired results. In any patient on whom it is necessary to remove thyroid tissue the following requirements are essential. First, we must have an adequate exposure of the field. This, in our experience, necessitates the cutting of the prethyroid muscles. Second, we must be certain that we remove sufficient thyroid tissue and that recurrence of symptoms does not take place a third time because of failure to remove an adequate amount of tissue. In the third place, it is obvious that we must leave sufficient tissue to provide the patient with the necessary thyroid secretion to maintain normal metabolism. As in all thyroid operations, it is, of course, imperative that we protect the parathyroid glands and avoid injuring the recurrent laryngeal nerve; that we see the trachea in order that we may not cut into it; and finally that we be constantly in a position in which we can completely control any hæmorrhage that may occur from the thyroid remnant.

The technique to be described has been developed in this Clinic and is now followed with satisfaction in dealing with all patients who require

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Fig. 1. The scar of the previous incision is completely excised. The knife blade is drawn sharply through all layers of the skin and subcutaneous fat at right angles to the surface. The skin flap is elevated by sharp dissection and by blunt retraction with gauze.

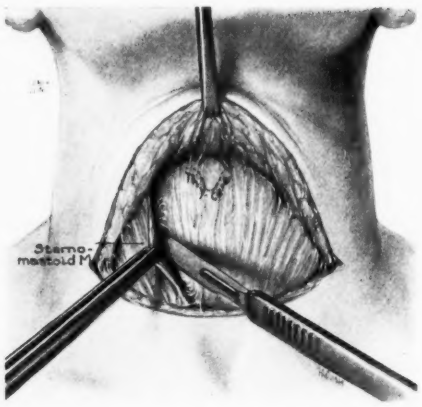

Fig. 2. The inner border of each sternomastoid muscle is dissected from the surface of the prethyroid muscles.

secondary operation for the removal of thyroid tissue. It is a striking fact that the success of many operations, particularly those in which the scar is visible after operation, is judged by certain people entirely upon the nature of the scar. For that reason, we have found that anything we may do to provide an elegant and sightly scar is most desirable. As shown in Figure 1, the first step in the operation is to excise the scar of the previous operation. We have found that considerable tissue may be safely removed without difficulty in later pulling the skin together. In excising the old scar the knife blade is drawn exactly perpendicular to the surface of the skin and is made to go completely through the skin and fat down to the fascia of the muscles over the thyroid gland. It is quite important that the line of incision through the skin shall be distinctly at right angles to the skin so that when the two edges are approximated they shall lie snugly against one another and thus give a good final scar. The skin flap is elevated in the usual manner by dissection with the knife blade through the area between the fascia overlying the prethyroid muscles and the fat of the skin flap. Furthermore, the skin flap may be elevated very considerably by wiping it up with a piece of gauze held in the thumb and finger. A line of cleavage persists for a long time following the previous operation and the entire flap can be very quickly and very completely wiped up to the desired height after it has once been started.

When the skin flap is elevated it is desirable to demonstrate very clearly on each side of the neck the inner border of the sternomastoid muscle. As shown in Figure 2, the sternomastoid is retracted with forceps and the inner border is demonstrated by a careful knife dissection. In this manner the entire muscle may be pulled backward from the underlying tissue, as shown in Figure 3. Deep beneath the sternomastoid will soon be seen the bulging internal jugular vein which is covered by scar tissue and by the fibers of the sternohyoid and the sternothyroid muscles at its lower end and by the omohyoid muscle in the upper part of the wound. The omohyoid muscle is an excellent landmark. It can be quite constantly demonstrated beneath the sternomastoid at the upper end of the incision. Very frequently we open only one side of the neck at a time when we are operating upon recurrent hyperthyroidism, because we find in these patients, as in the patients who are having their first thyroid operation, that the thyroidectomy must at times be divided into two stages. This division of the operation is necessary not only because of the severe hyperthyroidism which may be present but also because the technical difficulties are occasionally so great that they make it inadvisable to do more than half of the operation at a time.

When the sternomastoid muscle has been retracted and the omohyoid demonstrated as it overlies the internal jugular vein, the omohyoid is lifted from the internal jugular vein and the vein is carefully dissected throughout its length in the wound. The jugular must also be completely dissected from the side of the thyroid remnants as is shown in Figures 4, 5, 6. Of great assistance

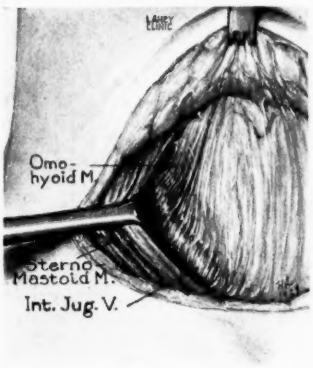

Fig. 3.

Fig. 3. When the sternomastoid is pulled widely back from the prethyroid muscles the omohyoid can be clearly seen in the upper part of the wound. In the depth of the wound are visible the blue, pulsating walls of the internal jugular vein which is lightly covered over by the adherent muscles.

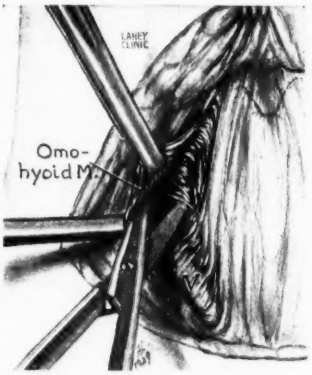

Fig. 4.

Fig. 4. With the sternomastoid retracted, the omohyoid is elevated and the superior and lateral surfaces of the jugular vein disclosed just beneath it.

Fig. 5.

Fig. 5. A double hook is inserted in the superior pole and the thyroid remnant rotated inward to facilitate dissection of the jugular vein.

in this maneuver is the rotation to the midline of the thyroid remnant by a properly placed double hook, as was suggested by Dr. F. H. Lahey some years ago. This part of the procedure is essential for the demonstration of the internal jugular vein and gives the most important landmark in the operation (Fig. 5). When we know where the internal jugular vein lies, we do not injure the vein; we see the lateral border of the thyroid remnant; we know where the parathyroids presumably lie; and we know where the recurrent laryngeal nerve is to be found. A great deal of time can justly be spent upon the adequate and careful separation of the jugular vein from the lateral surface of the thyroid remnant.

As soon as the position of the jugular vein and its relation to the lateral surface of the thyroid remnant is established, we are ready to separate the prethyroid muscles from the front of the gland. With the jugular retracted from the remnant of thyroid tissue with a special thyroid retractor, an Ochsner clamp is insinuated beneath the prethyroid muscles on the anterior surface of the thyroid remnant, as is shown in Figure 7. When the Ochsner clamp has been pushed through to the midline of the neck, two clamps are placed on the prethyroid muscles and a transverse incision is made between them, as in a primary thyroidectomy. The separation of the thyroid muscles from the thyroid remnant is now relatively easy but is best done in our experience with scissor dissection of the dense adhesions between the gland and the muscles. As the clamps are lifted from the surface of the thyroid remnant it is readily possible to free the under surface of the muscles from the gland. As the upper segment of the prethyroid muscle is raised toward the chin a place is generally reached where there has not been any previous dissection and there is a definite layer of loose areolar tissue which presents itself beneath the muscles at the superior thyroid pole. In this way, the entire superior pole is very soon directly in view and is marked out very clearly. To the outside is the internal jugular vein which has been retracted from the gland remnant.

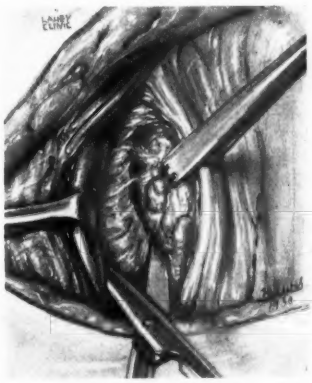

Fig. 6. The vein is here retracted with the sternomastoid, the outer border of the thyroid remnant is completely visible, and the prethyroid muscles are ready to be elevated from the front of the lobe.

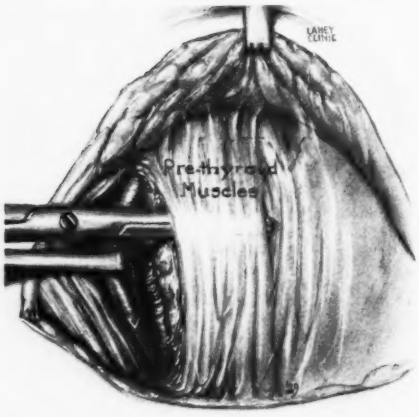

Fig. 7. The prethyroid muscles are elevated by inserting an Ochsner clamp beneath them—clamping and cutting them transversely in the center. Each portion of muscle must be carefully dissected from the face of the thyroid to the upper and lower limit of the remnant.

Above are the prethyroid muscles which have just been elevated. To the inside, lies the laryngeal cartilage and it is almost always possible to visualize the entire superior thyroid pole of the remnant with its blood supply. The muscle overlying the lower portion of the thyroid remnant must now be dissected downward. Its edge is held by an Ochsner clamp and its inferior surface is carefully cut away from the thyroid remnant. It is important that this muscle shall be dissected well down the neck until one is able to feel and see its attachment to the inner surface of the sternum. By the adequate section of the prethyroid muscles one may be certain he has a complete exposure of all the thyroid remnants. After we have removed very large thyroid remnants from the upper portion of the thyroid gland region we have repeatedly noted that there is still a large piece of thyroid tissue to be found at the lower pole well down at the sternal notch. Unless the prethyroid muscles are dissected downward from the gland and freed from the vein, it will not be possible to see this area. Furthermore, as these muscles are dissected downward to their attachment on the inside of the sternum it is noted that there is considerable loose areolar tissue in the midline of the neck which overlies the trachea. When this areolar tissue is visible, the trachea can be felt and in many instances can be seen in the midline of the neck at the sternal notch.

It is to be seen from what has already been said that a large part of thyroidectomy in recurrent hyperthyroidism is related to the exposure of the thyroid remnants. Unless a great deal of careful attention is paid to the dissection of the jugular from the side of the remnant and to the demonstration of the trachea in the midline and of the superior pole above, a safe removal of the remnant of thyroid tissue will not be possible. On the other hand, it is equally true that if all these structures are carefully demonstrated before the removal of any thyroid tissue is attempted, that an adequate amount of thyroid tissue can be readily removed in the manner of the usual primary operation. As is shown in Figure 8, double hooks are placed upon the thyroid remnant just as in a primary operation. At the superior pole the vessels are caught and clamped. At the side of the thyroid remnants, the vein is retracted and sharp clamps are pushed into the thyroid tissues. Notice in Figure 8 that the trachea is very clearly demonstrated in the midline by the deep reflection of the lower segment of muscle. Notice that a snap is in such a position over the front of the trachea that it separates the isthmus of the gland from the trachea and yet is placed so that it will not endanger any of the tracheal rings. It is obvious from Figure 8 that all the technique of primary thyroidectomy can be readily followed. An adequate piece of thyroid tissue can be left behind and sufficient thyroid tissue can be removed. Hæmorrhage can be completely and readily controlled by the folding over of the thyroid remnant after the major portion has been removed or by the dissection and ligation of the inferior thyroid artery beneath the internal jugular vein and carotid artery at the side of the thyroid remnant. The parathyroid glands which generally lie on the outer surface of the gland on the lateral and inferior surface of the lobe are protected by leaving tissue in this area whether or not they are visualized. The recurrent laryngeal nerve is protected as in the usual thyroidectomy by avoiding the area in which it runs.

The closure of the wound after the removal of thyroid remnants is carried out as in a primary thyroidectomy. The edge of the thyroid remnant can be folded over to the midline, as shown in Figure 9. Note that the stitches are so placed that they bring the edge up to the thyroid cartilage. It is desirable to avoid folding gland tissue over to the trachea, since it has been our experience that this may put sufficient pressure on the trachea to obstruct it. The uncut lateral extension of the sternothyroid muscle is extremely useful to fold in over the remnants of thyroid tissue to obliterate the dead space as well as to control any ooze which is still present. This procedure is

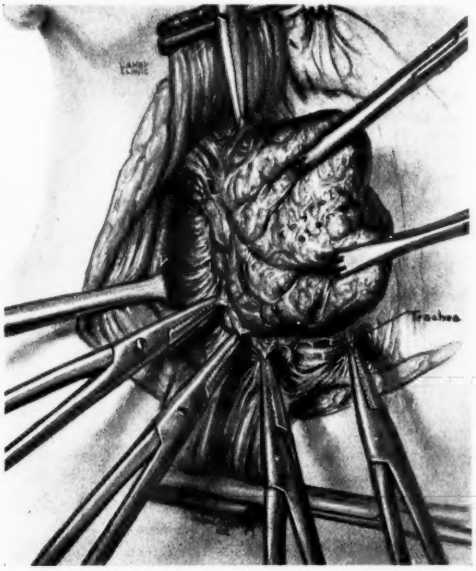

Fig. 8. The entire thyroid remnant being exposed by the retraction of the jugular and the separation of the prethyroid muscles, a subtotal hemithyroidectomy is done with the usual technique. The trachea can be seen and protected; the recurrent laryngeal nerve and the parathyroids avoided, and an adequate amount of thyroid tissue can be removed.

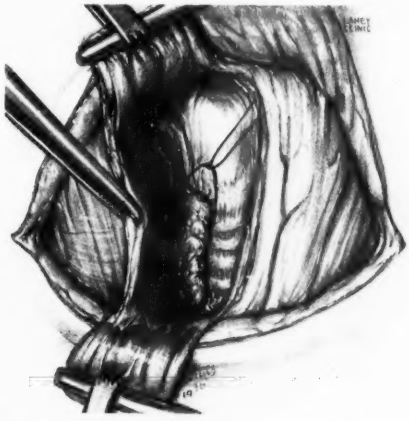

Fig. 9. Folding of gland remnant to midline. First suture in place to pull muscle tissue in over the remnant of thyroid tissue.

shown in Figure 9. Most of the oozing after thyroidectomy in recurrent hyperthyroidism comes from just beneath the skin flap; the actual operative field itself being almost always completely dry before it is left, so that drainage to the deep layers is not necessary. If, however, the gland surface oozes sufficiently to prevent control by folding or by placing raw muscle over it, we then insert a cigarette drain and place the gauze over the oozing surface. If a cigarette drain is used, however, we prefer that the drain emerge at the outer angle of the wound and that it enter the deep layers beneath the lateral incision in the prethyroid muscles. This gives drainage which is aided by gravity and provides that any interference with the healing of the scar will be in the least prominent part of the scar.

In the closure of the wound, the prethyroid muscles are sutured together with mattress stitches whenever it is possible. Frequently, however, the previous operation has made considerable scar tissue so that mattress sutures become somewhat difficult to apply and then ordinary interrupted stitches must be used for closing these muscles. The platysma muscle is not sutured, for we have found that this is not necessary if the skin is closed accurately with skin clips. One half of the skin clips are removed from the wound on the third day after operation and on the fourth day all the remaining clips are removed. This gives the smallest scar compatible with safety.

The most essential points in secondary operations for recurrent or persistent hyperthyroidism are adequate exposure by cutting the prethyroid muscles and demonstration and dissection of the internal jugular vein and common carotid artery from the thyroid remnant. With these two points accomplished, the procedure takes on the simplicity of the original subtotal thyroidectomy.

EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

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JULY, 1931

THE RELATION OF PSYCHIC MANIFESTATIONS TO CLINICAL INVESTIGATION

PSYCHOLOGY is a word widely used and often abused. In medicine applied psychology has its place as part of clinical investigation and is most valuable when there has been a previous acquaintance with the patient, but in diagnosis it must be taken in conjunction with the condition of the patient. Let us not forget that the signs and symptoms of the patient's disorder, meaning thereby the things that we can detect with our special senses, are the most valuable because they do not depend on the emotions of the patient.

Under proper conditions, applied by one who has had good medical training, psychological data have value, but the term psychology covers much loose thinking by men who have had little or no clinical training.

To ask a series of questions and then analyze the answers is often a hopeless task unless there is in addition material evidence of disease. So frequently we see the psychologist trying to evaluate an illness by an analysis of immaterial conversations held with the patient, as one would examine the blood or would seek other physical evidence—an attempt to give material consideration to immaterial phenomena.

The brain of man is an eye brain. The development of the gray matter of the hemispheres was coincident with the growth of vision. Always do we need to keep in mind in diagnostic evaluation, whether the evidences of disorder are such as can be detected by our special senses or whether they are symptomatic complaints or psychic phenomena. Careful evaluation is most essential for what we ordinarily call the neurasthenic patient.

Great care is necessary before advising operation in a wide range of disorders, especially those conditions in the abdomen which concern the position of the viscera. Many operations which have had no demonstrable relation to the patient's condition have been performed for so called ptosis of organs, and various doubtful abdominal disorders, usually with temporary relief, which is followed by a return of the symptoms, more operations, and more relief, until the sick habit has become confirmed.

There seems to be a conviction in the minds of many that the inside anatomy of the human body, within a small range of deviation, has a like configuration in all instances, yet we know that the position of the abdominal viscera varies greatly in different individuals. In the routine of examining patients for various conditions which do not concern the abdominal

viscera, one may find the pyloric end of the stomach in the lower abdomen, movable kidneys, prolapse of the spleen, and ptosis of various abdominal viscera, without any symptoms whatever.

As a matter of fact, people vary as much in the position of their internal organs as they do in the position of their external organs. If a blond man 6 feet tall came to us and said that he wanted to be a brunet 5 feet 10 inches tall, we should think that he was mentally deranged; yet series of operations have been undertaken to restore organs to a supposedly normal position, under the general theory that there was such a fixed normal position.

It is in this class of case that the shrewd, experienced practitioner must separate those material things which have a relationship to the complaint from those immaterial things which after all concern the emotional and psychic side of the patient's life. This problem most often arises with female patients who are social misfits. Some of them can be helped, but with others the condition is due to circumstances over which neither the patient nor the physician has control. Such patients may go to the hospital for an operation and improve greatly as the result of rest in bed and relief from responsibilities. On return home after a surgical vacation they are looked after more carefully, and perhaps have domestic help temporarily, only to relapse when the original conditions of life are re-established. It is in this type of case that the cults have their great field.

The wise medical practitioner, the family friend, is the man for the job, although we do not give to his method of handling the case the high sounding term of psychology. And in all conditions the nervous and mental reactions of the patient to the disease must be analyzed and carefully evaluated, but they must not be overestimated. W. J. MAYO

THE POTENTIAL MALIGNANCY OF WARTS AND MOLES

NO VARIETY of malignancy is more easily prevented than the type which has its origin in warts and moles. The predisposing lesions are superficial and therefore always evident. The factor of irritation, the one definitely established factor in the etiology of malignancy, is inevitable, is there for all to see, in these tiny growths which are always subject to the repeated insults, minor though they be, of scratching, of the friction of clothing, of the trauma of towel or comb or brush. The prophylaxis, complete excision of the causative lesion, is simple and absolutely sure. Yet people continue to die of the malignancy which develops from these lesions or must be subjected to extensive and mutilating operations for its cure, if they are fortunate enough to escape with their lives. Surely such a situation is disheartening proof of the inadequacy of our campaign for the control of cancer.

The majority of warts and moles are potentially benign lesions and tend to retain their benign characteristics regardless of the trauma to which they are subjected. But a small group is potentially malignant, and under repeated insults not only exhibits its malignant properties but sometimes proves very rapidly fatal. Twenty-five cases of this sort, with 10 deaths, were reported in 1904 by W. W. Keen, dean of American surgeons, in a paper read before the American Medical Association, and isolated instances of the same sort have been reported ever since, the latest, a peculiarly striking case because of the rapidly fatal outcome, by Kurtz of Philadelphia.[1] I have personally seen 5 such cases within the past 6 years, all of them originating from pigmented moles on the sole

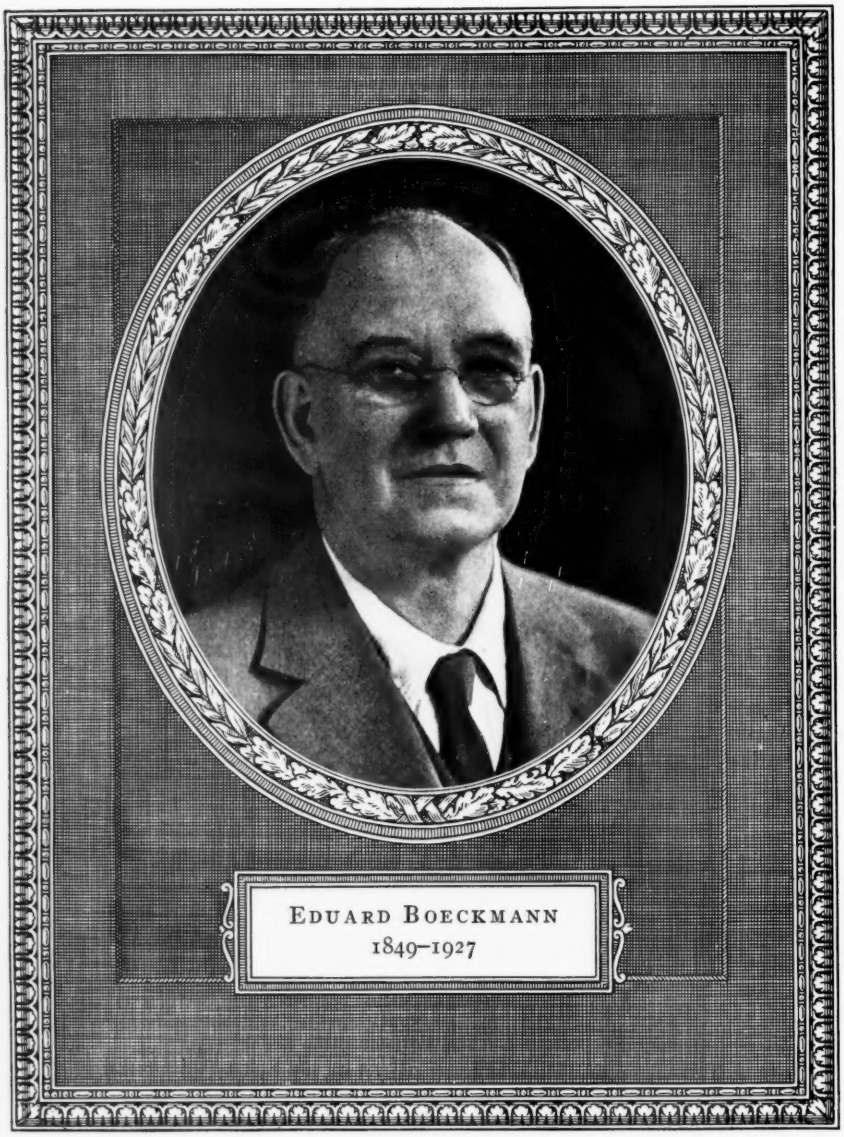
[1] J. Am. M. Ass., 1930, Nov. 22.

of the foot, all of them exhibiting a most malignant variety of sarcomatous change with widespread metastases, and all of them seen only when the malignant process was so far advanced that surgery of any sort was impossible.

The type of mole which originates in hypertrophy of the papillary layer of the skin tends to become carcinomatous, but excision, even when malignant changes have occurred, is frequently curative. On the other hand, the type of pigmented mole which exhibits enlarged and proliferating blood vessels can develop not only this variety of malignancy but also sarcomatous changes of a peculiarly uncontrollable and rapidly fatal character. The disease exhibits widespread metastases and multiple recurrences, and surgery is not only futile but actually seems to hasten the end.

We need to remind the public constantly, and we need to remind ourselves almost as often, that a mole, to quote Keen, "may be the match which starts a conflagration." Some warts and moles are potentially benign, some are potentially malignant. Some subjects who exhibit them are cancer susceptible, others are cancer immune. But we have no way of classifying either the lesions or the patients, and the only rational course of action, therefore, is to remove all warts and moles before they have developed their possibilities for harm, which they can do on any portion of the body and at any period of life—the fact that they have existed innocuously for years is no guarantee that they will remain harmless. It is positively not safe to delay removal until they have begun to enlarge or to manifest symptoms. Then the mischief is already done, the potentially malignant characteristics have become actually malignant, and attempts at removal frequently serve only further to disseminate the disease.

Removal before such a development, on the other hand, is a simple procedure by any method and particularly simple by electrosurgery, and in practically 100 per cent of all cases it is a procedure which terminates the menace forever. URBAN MAES.



EDUARD BOECKMANN
1849–1927

MASTER SURGEONS OF AMERICA

EDUARD BOECKMANN

IN the early days of medicine, among the men who were educated abroad and who brought their learning into the Northwest, Dr. Boeckmann occupied a very high place, not only as a practitioner of surgery, but as a teacher of the profession. We learned to know and to love him for his sterling qualities of mind and heart. It is to such men as Dr. Boeckmann and the late Christian Fenger that the profession owes a great debt, and I have requested that this short biography of Dr. Boeckmann be written that those of us who knew him may testify to his scientific leadership and the younger generation may not forget one of the old masters.

W. J. MAYO.

DR. EDUARD BOECKMANN, widely known ophthalmologist and general surgeon, died at Dellwood, White Bear Lake, Minnesota, on August 8, 1927, in his seventy-ninth year. He was one of the prominent medical men of the Northwest, and his notable contributions to medicine and surgery, with his unselfish devotion to his profession, were a source of inspiration to his many friends and colleagues.

Dr. Boeckmann was born in Totn, Norway, March 25, 1849, the youngest son of Daniel Peter Boeckmann, an officer in the Norwegian Army, and Eduardina Dreirer Boeckmann. He received his early education at private schools in Christiania, and entered the University in 1868. He was given his degree of Doctor of Medicine *cum laude*, in 1874. While a student at the University he received the Skjeldrup medal for research work on the anatomy, physiology, and pathology of the tonsils. After graduating from the University, Dr. Boeckmann was appointed assistant at the Lungegaard's Hospital for Lepers in Bergen, and the following year, physician in charge at St. Jorgen's Hospital, in the same city.

In 1882, he was given his Master's Degree in medicine by his alma mater for his thesis on "Keratitis Xerotica." About this time he made several trips to Copenhagen and Utrecht, studying ophthalmology with Grut-Hansen, Snellen, and Donders. After two visits to America, in 1882 and 1885 (at which time he practiced his profession in Chicago and in Minnesota), he brought his family, in 1887, and settled in St. Paul, where he lived for the remainder of his life.

He was a pioneer in scientific medicine and laboratory work. In the late eighties he brought to St. Paul his friend and former associate, Dr. G. A. Hansen, the discoverer of the bacillus of leprosy. Dr. Hansen worked in his office for over a year. Laboratory investigations in pathology and bacteriology with the aid of a microscope were at that time almost unknown to many members of the medical profession in the Northwest, and it may be of interest to note that work of this character was sometimes looked upon with suspicion.

Dr. Boeckmann's early contributions to medical literature were largely concerned with ophthalmology and were written in his native language. Among these were papers on "The Leprosy of the Eye," his own pterygium operation, and the "Treatment of Pannus by Periectomy." During the years that followed his coming to St. Paul, he wrote many papers on antisepsis, asepsis, methods of sterilization, etc. At that time he invented and patented a steam sterilizer, which was extensively used. One of his most important achievements was the perfecting of a method for preparing pyoktanin catgut for ligatures. He generously turned over the manufacture of this product to the Ramsey County Medical Society, in which he was deeply interested, and the profits from this industry constitute the major part of the now considerable fund which is known as the "Boeckmann Library Building Fund." The Ramsey County Medical Society also received from Dr. Boeckmann many contributions from his own library, and he was a generous supporter and adviser of the society for many years. He was one of the founders of the *St. Paul Medical Journal*, which, after 17 years of usefulness, was turned over to the Minnesota State Medical Association, and continued as *Minnesota Medicine*. It was to the former journal that Dr. Boeckmann contributed papers on "Transverse Incision in Abdominal Surgery," "Chronic Pancreatitis," and on many other subjects.

Dr. Boeckmann practiced medicine, in all its branches, with proficiency and skill, and contributed many original ideas and procedures to the art and science of medicine. He often made the statement that he was a country doctor practicing in the city. As his patients came from the entire Northwest, naturally many of them were of Norwegian extraction. His clientele was large and various, and as he made a practice of staying at his office until the last patient was seen, it was frequently late at night before he finished. Owing to his vigorous constitution and strength, he was able to stand this intense physical and mental strain.

As an ophthalmologist he was a recognized authority as a consultant, for, not only was he familiar with the thought and procedure of yesterday, but was thoroughly conversant with the ideas and practice of the present. Though conservative, he was ready to accept new methods, if his experience indicated need of such innovations. Dr. Boeckmann held European authority somewhat superior to American, but weighed all opinions against his own experience, which was based on an enormous number of patients and a long period of practice. His

opinion was recognized as final by his confrères without comment. "Dr. Boeckmann says," usually ended any argument. He was most generous in giving counsel to his colleagues, without compensation. Many younger men received much needed guidance from him, and this advice was given in a gracious and agreeable spirit. He was modest in deportment and undesirous of publicity. Neither envy, malice, nor covetousness had a place in his makeup. He listened kindly and attentively to others and gave his own opinion in such a way as to cause no humiliation or rancour. Dr. Boeckmann was liberal in his views of life and society, dispensed charity willingly, and was generous in his estimation of others; he was not given to unkindly criticism, either professionally or otherwise. Calm and deliberate in all his actions and speech, he, nevertheless, was occasionally annoyed by what might be considered trifles by others. He particularly resented anything derogatory to the land of his birth, even if said in jest, though his sense of humor was acute. He delighted in entertaining his friends and colleagues.

Dr. Boeckmann collected a gift of money among Norwegian Americans and others for the University of Christiania, in celebration of its one hundredth anniversary. The same year he was given a degree of Doctor of Philosophy by the University, and was made a commander of the Order of St. Olaf by the King of Norway. During the Spanish-American War he served as Major in the Medical Corps of the United States Army, in charge of a division hospital. He was one of the founders of the Bethesda and St. Paul Hospitals. The last years of his life he was a member of the staff of the Charles T. Miller Hospital.

Dr. Boeckmann was married in 1875 to Miss Anna Sophia Dorothea Gill. His wife and four children, three daughters and one son, survive him. Quoting from the writing of a friend in *Minnesota Medicine* of September, 1927:

> Nature had richly endowed him. That robust constitution permitted long hours of labor with little rest. From his early years to advanced age he worked long into the night. Frequently in the early morning hours he could be found studying scientific literature or in the preparation of medical works. Gifted with a brilliant mind, his faculty for clear and consecutive thought made him the great physician that he was. His originality, tenacity of purpose, dogged perseverance and independence of thought resulted in attainments for which he was widely known. He was possessed with an indomitable will and pride that were his heritage. His moral courage should be the envy of all men, for he feared no one. His intimates were few, his friendship enduring. In defense of a friend, he would stand alone, if need be, for his knowledge of human frailties made him the magnanimous spirit that knows no creed.
>
> His sincerity none will question; he was honest to a fault. Simple in manner and frank in expression, he had a rightful repugnance for ostentation and false show. He repelled the rich and invited the poor. He appraised the character and not the wealth.
>
> Charity was his religion. What greater virtue hath any man!
>
> EGIL BOECKMANN.

THE SURGEON'S LIBRARY

OLD MASTERPIECES IN SURGERY

ALFRED BROWN, M.D., F.A.C.S., OMAHA

THE SURGERY OF HENRI DE MONDEVILLE

IT is truly remarkable that the works of two of the greatest surgeons of the thirteenth century should have escaped the observation of both the medical men and the great printers of the Renaissance, especially as one of these surgeons, Henri de Mondeville, was the first native Frenchman to write a surgery.

It may be that the reason was that de Mondeville's work was never completed, for he died before he accomplished the task he had set himself and it may be that he was overshadowed by his student and successor, Guy de Chauliac, who treated de Mondeville about as he treated everyone else. One grows rather impatient at de Chauliac's constant derogation of nearly all the surgeons of his time. Regarding de Mondeville he says "Henri de Hermondavile at Paris commenced a very notable treatise in which he attempted to make a marriage between Theodoric and Lanfrancus, but being prevented by death, he did not finish the treatise." Reading a note of this kind the contemporary student would naturally pass the work by as only a fragment and of little importance and this is evidently what happened. It was not until 1892 that Dr. Julius Leopold Pagel published the latin text of de Mondeville's *Surgery* and a year later Dr. E. Nicaise with the collaboration of Dr. Saint Lager and F. Chavannes published his entire *Surgery*, translated into French. This revealed that in the treatment of wounds, at least, de Mondeville's ideas were far too advanced for his contemporaries to understand, and it was not until nearly three hundred years later that another surgeon of France, Ambroise Paré, was to rediscover them and put them in practice. In fact de Mondeville, being a better educated man than Paré and thus better able to reason logically was even beyond Paré in his wound treatment. He was sickly in his later years, however, and evidently did not have the requisite energy to insist upon his ideas, and his more aggressive student, de Chauliac, reverting to the ideas of the ancients popularized them so that the effect of de Mondeville's great teaching was lost. Both he and his work were forgotten.

Henri de Mondeville was born in Normandy some time during the early part of the latter half of the thirteenth century. Where he studied medicine is not known but, as he was a graduate in medicine and not one of the ignorant lay surgeons, it is fair to assume that he studied at Montpellier which was at that time the greatest school in France. Here he became a cleric and attained the rank of Master in Medicine.

Later he went to Italy and there studied surgery under the Italian surgeons and became greatly impressed by the ideas of Hugo de Lucca which were being taught by his son Theodoric. In 1301, de Mondeville is first mentioned as physician to the King, Philip the Fair, so he must have gained considerable reputation by that time. He accompanied the armies on their campaigns and there had the opportunity to try out the ideas of wound treatment he had learned from Theodoric in Italy. Evidently the results pleased him. He began to study wound healing and gradually evolved definite principles which later he incorporated in his book. Following the death of Philip the Fair in 1314, he became surgeon to his successor, Louis the Quarreler, but by this time was probably relieved from the duty of accompanying the army in its journeys and wars. He apparently preferred teaching. He was teaching at Montpellier in 1304 and began to teach at the University of Paris in 1306. During some of this period he was evidently working on his treatise for he says that in 1312 in Paris he read the first two chapters of his *Surgery* before "a large and noble assembly of medical students and other distinguished persons."

About 1316 his health began to fail and he tells us that he is fearful that he will not be able to finish his work. He made a brave fight but his prognosis proved correct and after finishing most of the *Surgery* he died, probably about 1320, leaving some of the chapters incomplete.

De Mondeville's great work was in the treatment of wounds. The current method was to enlarge wounds by tearing them and then filling them with tents, putting on remedies to promote suppuration, and dressing them frequently. Along with this the patients were almost starved until with the infection and starvation their condition was pitiful. "The ancients" believed also that wounds should heal slowly and under such treatment they must have been correct in their assumption. This method did not at all appeal to de Mondeville and he is most scornful of it. He says, "By this treatment more people die than are cured, and the treatment of those who recover is prolonged up to three months. . . . and the patient is always an invalid."

HENRI DE MONDEVILLE

D'après une miniature du manuscrit français 2030 de la Bibl. Nat. de Paris écrit en l'an 1314, du vivant de l'auteur.

REVIEWS OF NEW BOOKS

THE new, well illustrated text and reference book on *Diseases of the Skin* by Andrews[1] is worthy of a place in the study of the student or practitioner interested in dermatology and syphilology. It is up-to-date and distinctly practical.

The book is divided into 36 chapters, logically and uniquely arranged as follows: anatomy and physiology; etiology and pathology; symptomatology and general diagnosis; classification and terminology; principles of treatment; roentgen-ray therapy; supersoft X-rays; radium therapy; ultraviolet light; surgical diathermy; dermatoses due to physical causes; dermatoses due to local chemical irritants; dermatitis medicamentosa; erythema and urticaria; pruritus and cutaneous neuroses; eczema and allied conditions; psoriasis; lichen planus; vesicular and bullous affections; acne vulgaris; miscellaneous pyogenic infectious diseases due to fungi; tuberculosis cutis; other diseases due to bacilli; syphilis; diseases due to animal parasites; trophic disturbances; diseases of congenital origin; benign neoplasms; malignant neoplasms; the lymphoblastomas; diseases of the skin appendages; diseases of the mucous membranes; affections of the cutaneous blood vessels; anomalies of pigmentation; and tropical diseases of the skin.

The author's descriptions are, for the most part, concise and clear. He has incorporated in every chapter his own experience and opinion. He has, however, given freely of credit where credit is due, especially as evidenced by the bibliography at the end of each chapter, this containing references to most of the pertinent literature. Although brevity is a virtue, in places this has been practiced to such an extent as to make descriptions less lucid. Unfortunately, as is true with most dermatological textbooks, the histopathology has been somewhat slighted.

CLARK W. FINNERUD.

IN his book[2] entitled *Cancer of the Lung and Other Intrathoracic Tumours*, Maurice Davidson has given us a timely volume justified by the phenomenal post-war increase in the incidence of primary neoplasms of the lungs and bronchi. Formerly met with only rarely these lesions now make up from 5 to 10 per cent of all malignancies. Because of this fact and because in its different types and stages cancer of the lung can simulate practically every other chronic pulmonary affection, this excellent exposition of the subject fills a definite place in English medical literature. While the book is a practical text designed to make readily available the results of the extensive statistical, pathological, and clinical work which has been done on the subject, it has an ample bibliography and should be valuable to the specialist in pulmonary diseases as well as to the general diagnostician.

The chapter on diagnosis is especially good. The author stresses the necessity of considering it in all cases and of using every available aid in establishing the diagnosis. Among these he lists, besides the roentgenogram, bronchography, bronchoscopy, diagnostic pneumothorax, thoracoscopy, and exploratory operation.

The section on intrathoracic tumors other than cancer is too brief to be of great value and might well have been either omitted or improved.

JEROME HEAD.

THE laboratory guide by Nicholson[3] is intended as a vademecum for the practitioner who is isolated from university centers. Nevertheless it will be of interest to everyone. It contains a large amount of practical data presented in easily accessible form. One is impressed with a few rather unusual procedures intended to be short-cuts for the busy practitioner. The section on blood contains a good color plate of cells, including vital stained reticulocytes. The Price-Jones curve is emphasized, and a homemade halometer is shown. The section on blood chemistry includes directions for performing the usual determinations by simplified methods. There is a good section on biological reactions of the blood. In the bacteriological section, the typing of pneumonia by the urine method is given. The Fremont-Smith and Ayer table of differential diagnosis of cerebrospinal fluid findings is included. There are numerous photographs of urinary sedimenta. Basal metabolism technique is described. These selected examples indicate that this book is up-to-date and useful. It will be worth while to keep it at hand and use it.

PAUL STARR.

IN search of new anæsthetic methods, surgeons are confronted day after day, with new drugs and new methods of administration. These methods can survive, only if prolonged clinical trial proves their advantages over well recognized methods of inhalation and local anæsthesia. In a most timely contribution, the Surgical Clinic in Kiel[4] presents a six hundred page monograph on avertin (tribrommethyl alcohol). After so many enthusiastic or wholly deprecating articles, the impartial, critical attitude of this book makes it a real contribution in the history of anæsthesia. The chemistry and pharmacology of avertin, the premedication and dosage, together with various methods of adminis-

[1] DISEASES OF THE SKIN; A TEXTBOOK FOR PRACTITIONERS AND STUDENTS. By George Clinton Andrews, A.B., M.D. Philadelphia and London: W. B. Saunders Company, 1930.

[2] CANCER OF THE LUNG; AND OTHER INTRATHORACIC TUMOURS. By Maurice Davidson, M.A., M.D., B.Ch. (Oxon.), F.R.C.P. (Lond.). With a foreword by Arthur J. Hall, M.A., M.D., D.Sc., F.R.C.P. New York: William Wood and Company, 1930.

[3] LABORATORY MEDICINE. By Daniel Nicholson, M.D. Philadelphia: Lea & Febiger, 1930.

[4] DIE AVERTINNARKOSE IN DER CHIRURGIE. By Prof. Dr. W. Anschuetz, Dr. K. Specht, Priv.-Doz. Dr. Fr. Tiemann. Berlin: Julius Springer, 1930.

tration, the combination with other anæsthetics, the concentration of the solution and its absorption, the course of a normal anæsthesia, the untoward effects during and after narcosis and their prevention, the death reports and their critical analysis, and finally the present indications and contra-indications of this method are the most important chapters.

What is perhaps most instructive to the American reader, are the methods of arriving at a proper dosage, the proper organization of the personnel for such an anæsthetic, and the interesting contributions to the absorption of avertin from the lower end of the colon. Professor Anschuetz and his collaborators do not know whether this method is going to survive or not; whether it is going to be limited to certain operations, or whether it will be discarded as has the scopolamine twilight sleep. Nevertheless, they have done more than anybody else so far to stabilize the method. Their statistics and conclusions are based on the analysis of over three hundred thousand anæsthesias. The bibliography is complete up to the early months of 1930. The style is unusually clear and concise. The book is a very important contribution to surgical progress.

G. DE TAKATS.

THE preface of Benthin's *Gynecological Diagnosis*[1] opens with a veiled apology. Such a beginning is, psychologically, unsound. Moreover, the author requires no justification. To be sure, the medical student would not read a special work of 350 large pages, nor would the general practitioner acquire it, save the exceptional one who has the urge toward self-improvement. But there is a very definite need for just such a book for the younger generation of gynecologists, those who are still serving their apprenticeship or have only recently started their own practice; and even older and more experienced men will find much of value and interest in this work of a careful and judicious observer.

A subject of this sort hardly lends itself to detailed reviewing; yet, one cannot refrain from pointing out some of the statements which seem particularly new or praiseworthy. While the genital findings are obviously the starting point in making a diagnosis, the interrelations between the reproductive organs and the entire organism are so numerous and significant that the whole personality of the patient assumes great importance. Hasty diagnosis may lead to faulty indications for therapy, and often more than one examination is needed to clear up the situation. If we stop to consider how often operations are performed on the strength of *impression* rather than *diagnosis*, we must needs feel in agreement with the author. We must also underscore his warning against the traditional use of the uterine sound as a diagnostic aid, and agree with him that the practical value of salpingography is inferior to that of tubal insufflation. The chapter on the diagnosis of beginning general peritonitis which is as difficult as it is easy in advanced peritonitis, was to me of particular interest. Among the various diagnostic signs and symptoms described, the author lays particular stress on the dryness of the tongue; "if the *edges* of the tongue are dry, one hardly needs to seek further." One might, however, question the propriety of puncturing the abdominal wall, a procedure which he recommends though he is aware of the objections that have been made. As a final means of arriving at a diagnosis, he proposes exploratory laparotomy. "It is an heroic step . . . but it is better to open the abdomen once unnecessarily rather than to have caused irreparable harm by undue delay."

Wholly admirable and acceptable are the discussions on the differential diagnosis between hydrosalpinx and pyosalpinx, and between tubal pregnancy and other affections of the adnexa. A very good chapter, too, is the one on diagnosis during operation. In fact, the book is far from being a dry enumeration of signs and symptoms. It is written in a pleasing style, simple enough to render its study easy to American readers, enlivened by many very brief, pertinent case reports, supplied with 101 good charts and illustrations, and above all, beautified by 48 plates of truly excellent pictures in natural colors. The publishers deserve commendation for bringing out this book with its attractive make-up, at a very reasonable cost.

GEORGE GELLHORN.

NOT since Howard Kelly published his first gynecology has a book dealing with this specialty appeared which so closely reflects the viewpoint and the practice of its author as does Curtis' *Textbook of Gynecology*.[2] His personal opinions and ideas, based upon a rich clinical experience, and his own extensive and painstaking investigations, and his judicious comment upon what has been done by others, may be found all through the volume and give great value to a work which may well be considered an outstanding contribution to the gynecology of the period. The student will find here a very dependable textbook dealing with most of the problems encountered in practice today. To the experienced gynecologist it is a monograph which he will read with absorbing interest since it comes from a co-worker whose opinions are most highly esteemed and respected.

The first section is devoted to the infections. Under gonorrhœa the author emphasizes the harmfulness, as a rule, of active treatment of fresh infections, the self limited nature of salpingitis, the factor of re-infection as a cause of repeated attacks, and conservation in dealing with such lesions. Operations should be done largely to remove the pernicious results of such infections rather than the infection itself. At operation, whether a total or partial hysterectomy is done in addition to a salpingectomy the author places the ovaries toward

[1] DIAGNOSE UND DIFFERENTIALDIAGNOSE DER FRAUENKRANKHEITEN. By Dr. Walther Benthin. Berlin and Vienna: Urban & Schwarzenberg, 1930.

[2] A TEXTBOOK OF GYNECOLOGY. By Arthur Hale Curtis, M.D. Philadelphia and London: W. B. Saunders Company, 1930.

the side of the pelvis and rightly stresses the avoidance of tension upon the remaining parts and leaving them pliable—the danger of prolapse of the cervix or vaginal vault has been, he believes, overestimated. His emphasis upon this point is one of the most valuable lessons in the book.

Under the "cellulitis group" have been placed all non-gonorrhœal infections—quite a number of them including the puerperal. A very clear picture of them is thus presented.

There are excellent short chapters on genital tuberculosis, syphilis, and the non-specific (commonly) venereal infections.

The second section deals with tumors of the uterus. His estimate of the comparative value of radium and operation in the treatment of uterine fibroids—that in the main radium should be used only for women near the menopause with small bleeding fibroids, and when the health of the patient contra-indicates operation—seems eminently sound. Again he urges "adequate support without rigidity," in dealing with the vaginal vault or cervix in the concluding stages of a hysterectomy.

His chapter on cancer of the cervix is one of the best in the book. He stresses thorough search, which may include bisection of the cervix, in suspected cases—cancer of the endocervix may easily be overlooked. Bleeding is the paramount symptom in early cancer of the uterus and must be satisfactorily explained before ruling out this serious disease. The author uses radium combined often with surgical diathermy, except in cancer of the fundus in which instance hysterectomy is preferable.

The third section, devoted to tumors of the ovary, is a simple practical treatment of this subject, devoted conspicuously to the differential clinical diagnosis and the operative management.

The fourth section places before the reader a clear picture of the injuries created by childbirth, by following the course of the child from the beginning to the end of labor, and pointing out that we may not properly think of such injuries merely in terms of displacement of the uterus and a weakening of its supports, but regard all the tissues involved in the process. Examination should be directed to all injuries rather than to a few of the more commonly recognized ones. In repair he stresses the value of reconstruction of the pelvic tissues without undue tension, fixation, or rigidity. In the correction of the retrodisplacements, the author's usual procedure is silk suture of the uterosacral ligaments together with the Baldy-Webster operation and advancement of the bladder peritoneum upon the fundus. In selected cases an "angle-worm" reefing of the round ligaments, less often a modified Gilliam or Simpson operation, is used.

There is an excellent, detailed, illustrated account of the operation for prolapse, urethrocele, and cystocele, of the author's operations for perineal lacerations and rectocele.

In the fifth section are short chapters giving the pith of the prevalent ideas on dysmenorrhœa, uterine hæmorrhage, amenorrhœa, the menopause, sterility, and the endocrine disturbances from the gynecological aspect.

The sixth section gives an excellent résumé of Sampson's work on endometriosis.

Those interested in the now more than ever discussed question of chronic leucorrhœa will be interested in the background for study given in the author's short chapter on the subject. In his own investigations of a particular case the husband is interviewed and examined in all instances in which the leucorrhœa is of an infectious nature.

Genital fistulæ are discussed briefly, also backache, the disturbances of the pelvic veins, the physiology and pathology of the endometrium, and lesions of the cervix. Gynecologists are indebted to Dr. Curtis for calling attention to the frequent occurrence of cervical stricture and the rôle that it plays in pelvic pathology. "Just as we have learned to recognize that hæmorrhage after menopause is almost always diagnostic of uterine cancer, we may with equal assurance state that the otherwise inexplicable sudden appearance of profuse vaginal discharge in a woman well beyond the menopause is pathognomonic evidence of cervical stricture."

The volume is comparatively short, the bibliography has been well selected, the English clear and concise, and the book as a whole well worthy of this master gynecologist. To say that Tom Jones and Mary Dixon have furnished the illustrations means that nothing finer could be produced.

RICHARD R. SMITH.

THE work on *Dosage Tables for Roentgen Therapy*[1] is translated from the second German edition with the object of assisting the practical radiologist to estimate dosages without being obliged to go through the tedious physical mensuration and calculations necessary for the academically accurate measurements demanded by the physicist. The practical results obtainable by the dosage tables given in this little work are perfectly reliable within reasonable limits. Of course, these dosages relate to the physical quantities. As the author explains, whatever stress is placed on biological factors, we must always recall that the biological effect of the X-ray can be ascertained only quantitatively by using physical constants. These tables have proved very useful to all radiologists engaged in radiotherapy.

JAMES T. CASE.

THOUGH the literature on solid tumors of the ovaries is very extensive, there has been since 1910 no monographic treatise on this subject, except, perhaps, in the most recent large handbooks such as *Biology and Pathology of Woman* by Halban and Seitz. De Mora's book,[2] therefore, is a highly acceptable offering. It is based on 24 cases which

[1] DOSAGE TABLES FOR ROENTGEN THERAPY. By Professor Friedrich Voltz. Translated from the second German edition. London: Oxford Press, 1930.

[2] LES TUMEURS SOLIDES DE L'OVAIRE. By J. Luis E. de Mora. Paris: G. Doin et Cie, 1931.

have been studied very thoroughly both from the pathological and clinical aspects. Anatomically, the tumors are divided into four categories: connective tissue (fibroma, sarcoma, endothelioma); epithelial (carcinoma, chorio-epithelioma, folliculoma, wolffian ducts tumors, etc.); metastatic (Krukenberg tumor, secondary carcinoma); and heterotopic (teratoma, struma, hypernephroma). This first part of the book contains 15 plates with pictures of the gross specimens and photomicrographs.

The second part deals with the symptoms, complications, diagnosis and differential diagnosis, surgical and radiological treatment, the operative mortality and the final results. Throughout the book a very conscientious study of the literature of the world is in evidence. The diagnosis of a "solid tumor" of the ovary can be made without much difficulty in most cases; but the exact nature of such a tumor can, as a rule, be determined only at operation or on histological examination. Of the author's 24 patients, 22 were operated on; 6 by hysterectomy, 10 by unilateral, 4 by bilateral oophorectomy. There was no operative mortality, but the late results were less satisfactory; for only 9 women were alive at periods ranging from 1 month to 6 years after operation, respectively. A study of the literature, particularly that emanating from German sources, indicates that in malignant tumors of the ovaries which form the bulk of solid ovarian new-growths, postoperative radiotherapy improves the final results. This book is a very concise and complete survey of the subject.

GEORGE GELLHORN.

IN the preface of his book on *Physical Diagnosis*[1], Dr. Elmer states that he consented to revise Dr. Rose's book provided he could rearrange and rewrite the subject matter as seemed necessary to carry out his own ideas. This he has done by an entire rearrangement of the subject matter, which has been divided into parts.

Part I consists first of an excellent discussion of clinical anatomy and physiology. The normal physical signs are discussed and each method of examination in its entirety is covered before proceeding to the next method. This means that the divisions of inspection, palpation, percussion, and auscultation are covered with regard to the whole body rather than the usual one of covering each system. From a pedagogic view this appears logical. Added to the description of the normal physical findings is sufficient pathological discussion to bring out the relationship of the two. There are also chapters upon the polygraph and electrocardiograph covering the essential facts, as also one upon the use of the X-ray in physical diagnosis.

Part II consists of the application of physical diagnosis to disease.

The book is well written and should be of value to the practitioner and student. DON C. SUTTON.

[1] PHYSICAL DIAGNOSIS. By Warren P. Elmer, B.S., M.D., and W. D. Rose, M.D. St. Louis: The C. V. Mosby Company, 1930.

IN this latest edition, *Operative Gynecology*[2] by the two Drs. Crossen has attained the rank of a masterpiece. It is eminently fitting that so splendid a work in a special field which was literally originated and developed by American pioneers should be the product of American gynecologists.

The preface to this, the fourth edition, a cross section of the mental processes and attitude of the senior author, is a sufficient explanation of the outstanding position held by this text.

In spite of the very great number of titles, subtitles and further subdivisions in each major chapter, the whole is so well systematized with suitable chapter content outlines and general index that each detailed description is readily accessible. The inclusion of the author's preferences in this as in the previous edition must be of real value to those for whom the book must take the place of a senior consultant in making the choice of operative procedure.

The techniques described for linear cauterization of the cervix fail to make clear that the average lesion can be completely treated in one office session, by means of a long wire loop for the canal and a fine knife edge loop for the radial treatment of the cervix. Likewise the desirability of removing all mucus first, using strong bicarbonate solution or caroid powder followed by adrenalin for hæmostasis if necessary.

Diagnostic curettage in the non-pregnant uterus must be preceded by dilatation for which the author recommends the Goodell or similar power dilators carried to 1.5 or 2 centimeter dilatation. Mention should be made of the great advantage of the graduated snub-nosed Hegar set of dilators, curved metal cylinders ranging by 0.5 millimeters from 6 millimeters to 20 millimeters. A maximum size of 15 millimeters is ample for diagnostic use and increased dilatation with any instrument in the non-pregnant uterus must result in more or less severe splitting of the cervix.

The operative treatment of all types of abortion is omitted. The frequency of its occurrence, the tremendous morbidity and mortality incident to this condition make it imperative to emphasize in such a text as this the surgical principles involved, chief of which is digital exploration and separation of conception rests with the avoidance of the curette.

Among inhalation anæsthetics, ethylene-oxygen, which is far superior to nitrous oxide-oxygen, might have been included since the technique of administration has been developed to a degree of safety from explosiveness that places it on a par with other inhalation anæsthetics. For the sake of international comity the selection of cases illustrative of the medico-legal aspect of foreign bodies left in the abdomen could very well have been limited to American examples, for which the files of the *Journal* of the *American Medical Association* could serve as an abundant source. JOSEPH L. BAER.

[2] OPERATIVE GYNECOLOGY. 3d ed. By Harry Sturgeon Crossen, M.D., F.A.C.S., and ROBERT JAMES CROSSEN, M.D. 4th ed. St. Louis: The C. V. Mosby Company.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

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PRIMARY SYPHILIS IN THE FEMALE. By Thomas Anwyl Davies, M.D. London: Oxford University Press, 1931.

SPECIAL MEDICAL AND CLINICAL REPORT OF THE DEPARTMENT OF OBSTETRICS AND GYNÆCOLOGY, SIRIRAJ HOSPITAL, FACULTY OF MEDICINE, CHULALANKARANA UNIVERSITY, BANGKOK. For the Year Ending August 31, 1930. Bangkok, Siam: 1930.

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EASIER MOTHERHOOD. By Constance L. Todd. New York: The John Day Company, 1931.

THE DIAGNOSIS AND TREATMENT OF BRAIN TUMORS. By Ernest Sachs, A.B., M.D. St. Louis: The C. V. Mosby Company, 1931.

DISCOVERING OURSELVES; A VIEW OF THE HUMAN MIND AND HOW IT WORKS. By Edward A. Strecker, A.M., M.D., and Kenneth E. Appel, Ph.D., M.D. New York: The Macmillan Company, 1931.

CRIPPLED CHILDREN; TREATMENT AND ORTHOPEDIC NURSING. By Earl D. McBride, B.S., M.D., F.A.C.S. St. Louis: The C. V. Mosby Company, 1931.

THE SCIENCE AND PRACTICE OF SURGERY. By W. H. C. Romanis, M.A., M.B., M.Ch. (Cantab.), F.R.C.S. (Eng.), F.R.S. (Edin.) and Philip H. Mitchiner, M.D., M.S. (Lond.), F.R.C.S. (Eng.) 3d ed. vol. i, General Surgery; and vol. ii, Regional Surgery. New York: William Wood & Company, 1930.

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VERLAUF DER WICHTIGSTEN KNOCHEN- UND GELENKERKRANKUNGEN IM ROENTGENBILDE; EINE ANSCHAULICHE PROGNOSTIK. By Privatdozent Dr. med. Victor Hoffmann. Berlin: Julius Springer, 1931.

COLLECTED PAPERS 1904-1929. By Edwin Beer, M.D. New York: Paul B. Hoeber, Inc., 1931.

HEMORRHOIDS; THE INJECTION TREATMENT AND PRURITUS ANI. By Lawrence Goldbacher, M.D. 2d rev. ed. Philadelphia: F. A. Davis Company, 1931.

SURGERY; ITS PRINCIPLES AND PRACTICE. By Astley Paston Cooper Ashhurst, A.B., M.D., F.A.C.S. 4th rev. ed. Philadelphia: Lea & Febiger, 1931.

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DIAGNOSTIC METHODS AND INTERPRETATIONS IN INTERNAL MEDICINE. By Samuel A. Loewenberg, M.D., F.A.C.P. 2d rev. ed. Philadelphia: F. A. Davis Company, 1931.

PRACTICAL ANÆSTHETICS. By Charles F. Hadfield, M.B.E., M.A., M.D. 2d ed. New York: William Wood and Company, 1931.

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LA TACTIQUE OPÉRATOIRE. Published under the direction of M. Robineau and W. Stern. TACTIQUE OPÉRATOIRE DES ANNEXES DE L'UTÉRUS. By Raoul Charles-Monod. Paris: G. Doin & Cie, 1931.

AMERICAN COLLEGE OF SURGEONS

THE DUKE FOUNDATION IN RELATION TO MODERN HOSPITALS AND THEIR RESPONSIBILITY TO THE PUBLIC AND THE MEDICAL PROFESSION

FRANKLIN H. MARTIN, M.D., F.A.C.S., CHICAGO
Director General, American College of Surgeons

IT is inspiring for a modern Yankee to be invited to the Carolinas. Carolinians, from the beginning of our country and long before, have done their own thinking; and in our fight for independence their thinking was backed by an action that made them influential in that group of thirteen of which they were a part. At all times their culture, their social proclivities, and their educational ambition has placed them in a class by themselves in this Empire of the South.

Particularly am I glad to be a guest of North Carolina where live a group of my most valued friends. One of your greatest surgeons was a tower of strength to me in the organization of the General Medical Board of the Council of National Defense during the Great War—Dr. Hubert A. Royster.

One more friend, a neighbor of yours who has surprised us and honored us by his presence this evening, I cannot refrain from mentioning—Mr. Josephus Daniels. For nearly two years I was associated with him in the meetings of the Council of National Defense. We found him to be (I quote from my Diary) a keen, quiet man who attended strictly to his own business and whose most prominent personal characteristic was his very great modesty. He quickly, without apparent effort, won his way into our inner recesses and he was early counted as someone to tie to as a real friend and whom one would always find a willing and sympathetic counselor.

His opinions were pointedly and clearly stated, and of course without any appearance of embarrassment. And in accomplishments he was a past master. His department was driven by him instead of the reverse. He had the training of a newspaper editor and manager—the paper was always out on time and distributed before most people were up.

In our important discussions, when departmental activities were being considered, and his work was brought forward, we soon learned to say: "We don't have to bother with that. It pertains to Secretary Daniels' department."

His modesty, his great accomplishments, his broad vision, and his defense of principles won our admiration. And when the final history of the Great War is written, Josephus Daniels will be recorded as outstanding among our great Secretaries of the United States Navy.

Secretary of War, Newton D. Baker, whom we all also admired, was known as the "little giant"; and Secretary Daniels, in distinction, was affectionately dubbed the "silent giant."

JAMES BUCHANAN DUKE

And now we come to look upon the work of another North Carolinian—to view its far-reaching immensity, to admire, and to applaud.

James Buchanan Duke was well named. By his vision he has proved that he was not only a Duke, but a sovereign—an accomplisher of things, a servant of mankind. Here about us is the evidence in substantial beauty of his vision and his practical philosophy. Irresistibly the indicator of the medical center is moving toward the South. And the enviable standard of your hospitals will be further enhanced if full advantage is taken of existing opportunity.

All of the money in the world, however, will not create a great medical center. It required the activity of the Big Four of Hopkins—Welch, Halsted, Kelly, and Osler—to place that institution on the map. Here we have a like beginning with W. S. Rankin and Wilburt C. Davison whose responsibility is stupendous.

BEGINNING OF HOSPITALS

Hospitals had their beginnings in the earliest days, when the shade of the low wall or the tree by the roadside was utilized by the wayfarer, and it was here that the worker or the pilgrim stopped exhausted in his illness and was cared for by his companions. If it were cold, the protected cave

open to the sun, would be sought. Near by would be a spring, a pool, and running water, where the ill one could slake his thirst and bathe his body. When his fever had subsided and his illness had passed and the refreshed stranger was on his way, he would look back to his temporary refuge, tell his companions of his sojourn there, and of his recovery. It became the first hospital, a place of healing, a pool of Bethesda.

Hospitals had their beginnings when the warrior of old fell from the ranks, wounded or exhausted, and was cared for in some secluded glen by those of his fellows who were less severely stricken; they bound up his wounds, quenched his thirst, and gave him food. Hospitals had their beginnings when the pyramids were being built, and the master workmen were stricken or injured. There on the banks of the Nile, protected from the sun of the desert by the shade of a hut, they were restored to strength.

Hospitals had their beginnings when the children of Israel fled from Egypt and their followers fell by the wayside in their weary trek, and when in their illness they were nursed back to health in the protection of a friendly rock, or were buried by unselfish hands. Hospitals had their beginnings in the dwellings around and about Jerusalem, when Christ healed the sick. They had their beginnings in the monasteries of the early Christian days, and later in the rooms provided for the poor and the sick by the Bishops.

The Modern Hospital

We of this country, and our neighbors to the north, the Canadians, have done much to develop the practical hospital for men and women of whatever class. When we speak of medical service in hospitals, the question of rank should not be a consideration. People in hospitals are individuals without property, except that they have a bed to rest upon, a blanket to cover them, a light shift to conceal their nakedness. They are like the newborn babe. Therefore, we and the Canadians do not segregate according to rank. We have general hospitals where rich and poor alike may receive medical service, and where the members of the medical profession can conveniently and thriftily care for all of their patients under one roof, and give each and all of them the advantage of the same management, the same apparatus, the same nurses, orderlies, etc.

Many of you may not realize that in the older countries century-old traditions obtain, and that their great hospitals are available exclusively to the poor. These traditions were built up when hospitals were a refuge for the poor, when medical and surgical treatment was confined exclusively to emergencies, and before elective medicine and surgery had developed to the present proportions. Concurrently with the advent of modern surgery, medicine, and obstetrics, nursing homes were established to care for the well-to-do patients, or their homes were transformed at great expense and trouble into substitutes for hospitals. The King, a member of Parliament, or a cabinet minister of Great Britain could not legally become a patient in St. Bartholomew's or Guy's Hospital of London where every modern hospital facility is available to the poor.

Fifteen years ago the American College of Surgeons undertook the survey and betterment of hospitals. It was a stupendous task. To insure effective work, it was necessary to devise a standard that would meet the criticism and secure the acceptance of hundreds of independent hospitals. Thus a *minimum standard* was formulated rather than an *ideal one*. Two years of study, of comparisons, and of adjustments of hospital conduct were necessary before the present Minimum Standard was announced. It has stood the test of time and criticism for fourteen years, and it has stimulated the adoption of an *ideal* standard.

Most of you are familiar with the story of the application of this standard, year after year since 1918. The College engaged the services of graduate physicians who visited the hospitals of the United States and Canada and made personal surveys. Each year the College announces the hospitals that have warranted its approval. Dr. Malcolm T. MacEachern is the associate director in charge of Hospital Standardization.

At the annual meeting in 1930 the College presented a summary of the thirteenth survey as follows:

1. Hospitals of 100 beds and over:

Surveyed	1,433
Fully approved	1,272
Conditionally approved	62
Total fully and conditionally approved	1,334
Total percentage fully and conditionally approved	93.1

2. Hospitals of 50 to 100 beds:

Surveyed	1,001
Fully approved	482
Conditionally approved	114
Total fully and conditionally approved	596
Total percentage fully and conditionally approved	59.5

3. Hospitals of 25 to 50 beds:

Surveyed	730
Fully approved	82
Conditionally approved	51
Total fully and conditionally approved	133
Total percentage fully and conditionally approved	18.2

MINIMUM STANDARD FOR HOSPITALS

1. That physicians and surgeons privileged to practice in the hospital be organized as a definite group or staff. Such organization has nothing to do with the question as to whether the hospital is "open" or "closed," nor need it affect the various existing types of staff organization. The word *staff* is here defined as the group of doctors who practice in the hospital inclusive of all groups such as the "regular staff," the "visiting staff," and the "associate staff."

2. That membership upon the staff be restricted to physicians and surgeons who are (a) full graduates of medicine in good standing and legally licensed to practice in their respective states or provinces, (b) competent in their respective fields, and (c) worthy in character and in matters of professional ethics; that in this latter connection the practice of the division of fees, under any guise, whatever, be prohibited.

3. That the staff initiate and, with the approval of the governing board of the hospital, adopt rules, regulations, and policies governing the professional work of the hospital; that these rules, regulations, and policies specifically provide:

(a) That staff meetings be held at least once each month. (In large hospitals departments may choose to meet separately.)

(b) That the staff review and analyze at regular intervals their clinical experience in the various departments of the hospital, such as medicine, surgery, obstetrics, and the other specialties; the clinical records of patients, free and pay, to be the basis for such review and analysis.

4. That accurate and complete records be written for all patients and filed in an accessible manner in the hospital—a complete case record being one which includes identification data; complaint; personal and family history; history of present illness; physical examination; special examinations, such as consultations, clinical laboratory, X-ray and other examinations; provisional or working diagnosis; medical or surgical treatment; gross and microscopical pathological findings; progress notes; final diagnosis; condition on discharge; follow-up and, in case of death, autopsy findings.

5. That diagnostic and therapeutic facilities under competent supervision be available for the study, diagnosis, and treatment of patients, these to include, at least, (a) a clinical laboratory providing chemical, bacteriological, serological, and pathological services; (b) an X-ray department providing radiographic and fluoroscopic services.

4. Government hospitals:

(a) Army:	
Surveyed	5
Fully approved	5
Percentage fully approved	100
(b) Navy:	
Surveyed	13
Fully approved	13
Percentage fully approved	100
(c) Public Health Service:	
Surveyed	24
Fully approved	24
Percentage fully approved	100
(d) Veterans Bureau:	
Surveyed	49
Fully approved	49
Percentage fully approved	100
(e) National Homes for Disabled and Volunteer Soldiers:	
Surveyed	10
Fully approved	10
Percentage fully approved	100

5. Other Countries:

Twenty-five hospitals of other countries have been awarded full approval, and are included in the list of Approved Hospitals for 1930 (Australia, China, France, Newfoundland, New Zealand, and Uruguay).

SUMMARY

Total fully approved	1,836
Total conditionally approved	227
Total fully and conditionally approved	2,063
Total not approved	1,101
Total surveyed	3,164

The Model Hospital

May I now suggest to this Duke Foundation, which has accepted the hospital leadership in these two commonwealths, an amplification of its program which will consider the establishment and conduct of hospitals with more far-reaching activities than those commonly performed by our present approved institutions. The profession of scientific medicine, with the modern demand upon it for varied and costly scientific equipment and skilled medical aids and technicians, is rapidly losing its position of power and independence.

The public is confused. The family adviser—the family doctor—in many communities is difficult to find. If occasionally he is discovered it is apparent that he has become the head of a com-

HEALTH INVENTORIUM

THE REQUIREMENTS

The hospital should furnish an examining room or rooms, to which any legalized practitioner (who is a member in good standing of the American Medical Association and of his respective county medical society, of the Canadian Medical Association and its subsidiary branches, or similar medical organizations in the South and Central-American Republics who accept the advice of the American College of Surgeons) may bring a patient for examination.

The hospital should furnish to the practitioner every facility in the way of aids, consultants when necessary, laboratory tests, etc., as will insure a comprehensive audit of his patient's condition. The charge for the required laboratory tests should be nominal, and the maximum not to exceed actual cost. There should be no charge for the use of the examining room. The physician should render to the patient (if he is able to pay) a bill covering the fee for the examination, and where there is a charge for laboratory services, he should be responsible to the hospital for its payment.

SAFEGUARDS

1. To insure protection to the practitioner, no hospital should accord these facilities to any individual who is not accompanied by his or her doctor, or who does not carry a letter from his or her doctor in which certain services are requested.

2. An individual who applies for an examination and who has no physician should be referred to a duly appointed, distinterested committee consisting of a representative or representatives of the local medical society and the standardized hospitals of the community, and this committee should advise the patient in the selection of a physician.

3. Each hospital volunteering to establish such facilities will be accredited as conducting a Health Inventorium.

prehensive machine, or he is outclassed by a combination of time servers.

Most of the qualified practitioners who graduated in medicine within the last thirty years received the degree of M.D. from Class A medical schools, affiliated with endowed universities of the United States or Canada. They served one or two years as internes in approved hospitals and their study and training were not confined to one specialty but embodied all branches of medicine.

Upon graduation they are confronted with the decision to accept or refuse attractive positions—ready-made service as salaried aids in the field of public health or in philanthropic foundations; as full-time aids or assistants in endowed dispensaries, or university clinics; as health administrators of hospitals, or private health organizations; as professional guides in publicity of health guilds or charitable organizations; or possibly as medical or surgical administrators of industrial plants. Organizations of this type, and others too numerous to mention, offer an immediate fixed salary, and furnish offices with willing aids who will lend dignity to the positions. Alluringly these inducements are urged for consideration.

If the young graduates resist the temptation of these attractive salaried positions, they are aware of the obvious fact that even though they possess the necessary training, they cannot be proficient in all branches of scientific medicine without suitable apparatus and laboratory facilities. To maintain their independence, where could they receive such aid to better advantage than in an approved hospital?

A solution of the independent practitioners' problems reveals an added function for the community hospitals that are supported by private and public funds. It reveals the fact that the hospital has all the requirements in laboratories, scientific apparatus, and trained technicians and medical aids that are the boast of the most approved diagnostic clinic. Hence the College has suggested to the approved hospitals that they extend their diagnostic facilities to independent qualified practitioners of scientific medicine through a department to be known as a "Health Inventorium." (Approximately forty per cent of the independent family doctors of the United States and Canada are already members of hospital staffs. The remaining sixty per cent should have the facilities of a "Health Inventorium.")

And what hospital would suffer professionally, financially, or scientifically by extending the privilege of a diagnostic clinic to every modernly educated doctor? What community of people would not be benefited by this extension of hospital privileges to their own family doctor? And of the *greatest importance*, what other method can be devised that will save the independent medical practitioner from extinction, and our profession

MINIMUM STANDARD FOR CANCER CLINICS

1. *Organization.* There shall be a definite organization of the service, and it shall include an executive officer and representatives of all the departments of the hospital which are concerned in the diagnosis and treatment of cancer. The services of a secretary and of a social service worker shall be available.

2. *Conferences.* As an essential feature of the service there shall be regular conferences or consultations at which the diagnosis and treatment of the individual cases are discussed by all members of the clinic who are concerned with the case.

3. *Patients.* Reference to the cancer clinic of all patients in whom the diagnosis or treatment of cancer is to be considered shall be either voluntary or obligatory in accordance with the vote of the medical staff or of the governing board of the hospital.

4. *Equipment.* In addition to the diagnostic and therapeutic surgical equipment which is required in every approved general hospital there shall be available an apparatus for X-ray therapy of an effectiveness generally agreed upon as adequate, and an amount of radium sufficient to insure effective treatment.

5. *Records.* In addition to the records which are required in every approved general hospital, there shall be additional records of: (a) The details of the history and of the examination for cancer in different regions of the body, such as are indicated on the form records which are recommended by the Committee on the Treatment of Malignant Diseases, American College of Surgeons. (b) The details of the treatment by radium or X-ray as indicated on the form records which are recommended by the Committee on the Treatment of Malignant Diseases, American College of Surgeons. (c) Periodic examinations at intervals for a period of at least five years following treatment.

6. *Treatment.* The treatment of cancer patients shall be entrusted to the members of the staff of the cancer clinic except in cases in which adequate treatment in accordance with the collective recommendation of the staff of the cancer clinic can be procured otherwise.

from dependency, commercialism, state control, or socialism?

The plan of administration that the College suggests to hospitals is as follows:

First: Furnish diagnostic facilities to all educated, licensed graduates in scientific medicine through Health Inventoriums.

Second: Furnish facilities for the diagnosis and treatment of cancer, through organized cancer clinics.

Third: Furnish in all communities facilities for the care of the injured, in and out of industry, through organized traumatic clinics.

Health Inventorium

Five years ago the American College of Surgeons developed a plan which would furnish to the doctor of every community the necessary equipment, laboratory facilities, and trained aids that would enable him to compete in scientific accuracy with his more fortunate fellow practitioners who have hospital or organized clinic affiliations, and give him ready access to all of these necessities.

The College's announcement read: "A diagnostic clinic in every community; the family physician furnished with diagnostic facilities similar to those accorded to the attending staffs of most approved clinics or hospitals."

Periodic Health Examinations

Every intelligent individual now realizes the importance of submitting himself or herself to a health audit or examination at least once each year. This procedure has been advocated by health societies; it has been preached from lay platforms and church pulpits; it has been recommended by authors of health columns, and it has been earnestly advised by the family doctor.

The majority of people who are inclined to accept this advice have family physicians upon whom they depend in time of sickness. In considering the periodic health examination, naturally they turn to these same family doctors. But without the apparatus of precision, the family doctor is unable to make a complete survey of his patients or record complete findings. No educated physician should be subjected to this embarrassment.

The Plan

There are more than 3,200 hospitals in the United States and Canada that are under survey by the American College of Surgeons. Of these, 2,063 are known as "standardized" institutions and others are rapidly qualifying.

A careful yearly survey of hospitals is conducted by the College, which has furnished the Minimum Standard. The estimate of the hospitals

MINIMUM STANDARD ON INDUSTRIAL MEDICINE AND TRAUMATIC SURGERY

1. That all hospitals receiving traumatic cases for treatment be required to meet the minimum standard requirements of the American College of Surgeons.

2. That each of these hospitals shall have a committee responsible for the supervision of traumatic surgery.

3. That a surgeon approved to treat traumatic cases shall be: (a) a graduate of scientific medicine in good standing and licensed to practice in his respective State or province; (b) competent in the field of traumatic surgery; (c) worthy in character and in matters of professional ethics; that in the latter connection the practice of division of fees under any guise whatever be prohibited.

4. That surgeons dealing with traumatic cases shall keep accurate and complete clinical record of all patients—in accordance with the minimum requirements of the American College of Surgeons, paying special attention to the immediate record of injury, detailed description of physical findings, adequate record of treatment, a record of estimated period of disability, the end-results when possible; and these records shall be filed so that they are available at all times for submission as shall be required.

5. That all surgeons and hospitals dealing with traumatic cases shall have available adequate diagnostic and therapeutic facilities.

that are qualified is determined by this survey, the results of which form the basis of the annual report to the public. Each standardized hospital can furnish the practitioner with the necessary equipment and aids to insure the comprehensive examination of a patient. Such facilities are already furnished by many hospitals, especially community hospitals, to the legalized practitioners within their districts.

Cancer Clinics

It appears self evident that at least one standardized hospital in each community should maintain an approved cancer clinic, whose facilities and services would be available to all scientific doctors.

The Committee on the Treatment of Malignant Diseases of the American College of Surgeons, under the chairmanship of Dr. Robert B. Greenough of Boston, and Associate Director Bowman C. Crowell of the College, has been a leader in this work for fourteen years, has made yearly reports of progress, and has announced a concrete standard for Cancer Clinics, particularly applicable to approved hospitals.

This standard speaks for itself.

The Duke Foundation, with its existing plans for hospital organization, could very properly take the lead in providing cancer clinics in which all independent physicians could have access to the facilities for diagnosis and treatment of their patients under the supervision and guidance of an organized cancer service.

Industrial Medicine and Traumatic Surgery

A Minimum Standard on Industrial Medicine and Traumatic Surgery was formulated by the American College of Surgeons in 1926. It was the outcome of meetings on several successive days which were participated in by outstanding lay and medical leaders in industry, in labor, in indemnity insurance, and industrial physicians and surgeons.

The standard has been carefully studied by officials representing industry, labor, insurance companies, the medical profession, hospitals, and administrators of State compensation laws; and in principle it has been approved by all of them. With the co-operation of medical representatives in industry, the working details have been perfected, and the College is now ready to aid in the establishment of model departments along these suggested lines and to assist in perfecting any comparable services as are already in existence. The College is enlisting the co-operation of the 2,063 hospitals on its approved list, in this far-reaching program, the importance of which cannot, in my opinion, be exaggerated.

Dr. Frederic A. Besley is the chairman of the Board on Industrial Medicine and Traumatic Surgery.

High Cost of Medical and Surgical Care

The high cost of medical and surgical care has been the subject of much recent discussion and of many great conferences. With but few exceptions the resulting recommendations which promise lower costs of treatment tend to eliminate the independent practitioner of medicine. Why? Because the independent family doctor cannot duplicate the expensive apparatus and therapeutic facilities that are available to his more fortunate fellow practitioners who are on the staffs of approved hospitals; equipment that is essential if

he is to furnish the highest type of service to his patient. Here is where influential organizations like the Duke Foundation can render most valuable aid to the independent doctor by encouraging the hospitals under their jurisdiction to establish Health Inventoriums. Other approved hospitals will follow the example of such action, when it is observed that it will extend valuable service to the public and to the independent physician, and lead to advantages that will not only enlist universal approval, but also financial support.

Of the 168,000 physicians and surgeons recorded in the United States and Canada, who have graduated in scientific medicine and earned the degree of M.D., the independent family physicians number about 100,000. The remaining medical graduates comprise the practitioners who are rendering valuable and necessary service as salaried public health officials of the government, the State, the county and the municipality, and semi-philanthropic organizations; the Army, the Navy, and the Marine Corps; public and private group clinics for diagnosis and treatment; full time teachers in medical schools; resident physicians in hospitals, administrative and professional; internes and hospital superintendents, medical and surgical administrators in industry, and doctors who have retired, voluntarily or for other reasons, from the practice of medicine.

Hence the independent practitioner upon whom we must depend for personal advice and personal visits—the family doctor—approximates sixty per cent of the independent scientific medical profession. He alone depends upon his own efforts to support his family, and his paramount interest is in the practice of medicine as a profession among the families of his community.

Summary

1. Prevention has become an outstanding factor in medicine. The people are more and more interested in the practical application of preventive measures in dealing with personal health. They realize that more than one-third of our boys who were examined for service in the Great War were declared to be unfit.

Twenty-five years ago but a scattering few appreciated the advantages of a periodic health examination, whereas millions are now demanding this service. The increase in health audits ranges in some communities from 100 to 1,000 per cent.

The majority of the people prefer to go to their own family doctor for these examinations. This desire is so universal, and the beneficial results of the examinations are so obvious, that the general practitioner is now called upon to apply preventive as well as curative measures in his every day practice. What greater and more appropriate service could the Duke Foundation render to the people and to the profession than to establish model Health Inventoriums?

2. The public is mindful too of the great menace of cancer, and of the fact that this disease, with its annual toll of approximately one hundred and forty thousand individuals, can be prevented if it is discovered early and proper treatment applied. Cancer clinics in community hospitals will give the people and their physicians every modern facility for scientific examination, and the most approved methods of treatment. What would be more appropriate than that the Duke Foundation should establish such cancer clinics as models for all approved hospitals?

3. The industries great and small, those serving in industry, and physicians who are called upon to care for the thousands of traumatic cases outside of industry, are seeking opportunities for better service. Some of the larger industries already provide such facilities to their people. Who can better aid in giving service to the smaller industries than the community hospitals? Thousands of traumatic injuries occur outside of industries. Who can better provide appropriate and economical service in these cases than these same community hospitals?

These problems are acute. The American College of Surgeons is in dead earnest in its desire to help in solving them, in its desire to enter into partnership with all modern hospitals, in its desire to aid the educated practitioner of medicine to obtain economical facilities for his work, and in its desire to reduce the cost of medical care to the people by *supporting* the independent doctor instead of eliminating him.

In this partnership of course we of the American College of Surgeons hope for the enthusiastic cooperation of the Duke Foundation.